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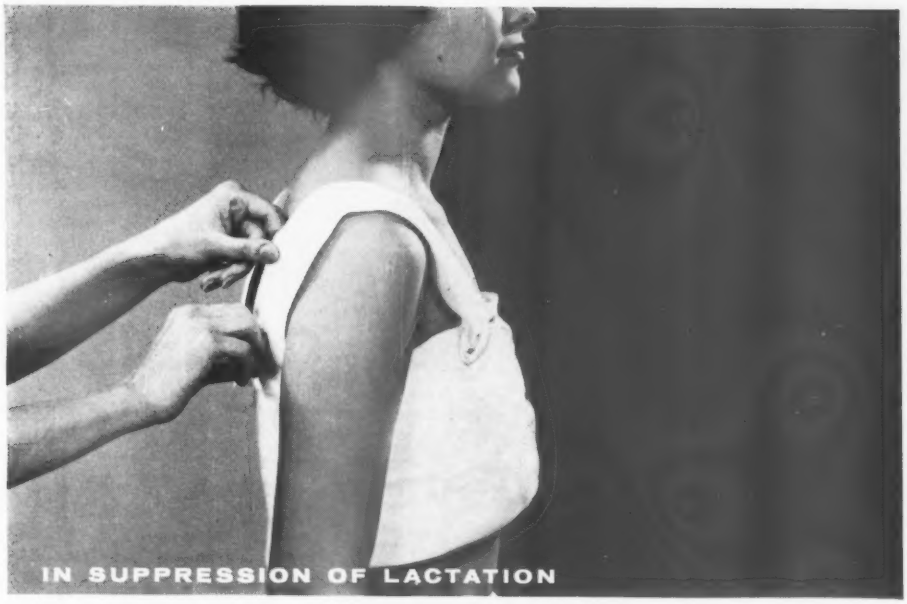

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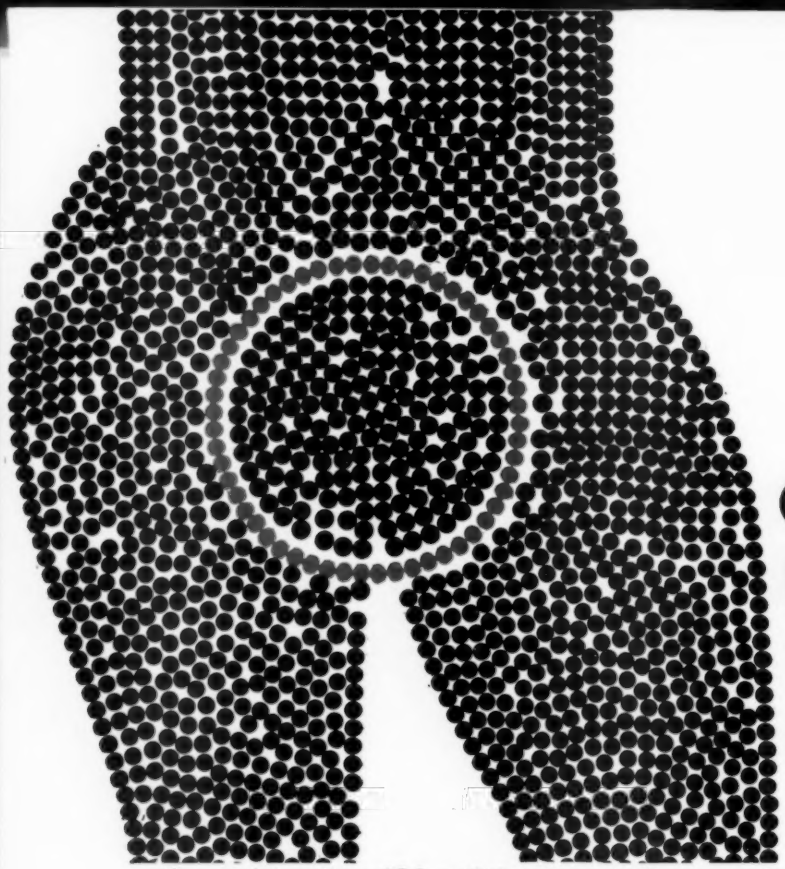

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References: 1. N. Mulla and J. J. McDonough, Ann. New York Acad. Sc., 82: (Art. 1), 182, 1959. 2. L. E. Savel, D. B. Gershenfeld, J. Finkel and P. Drucker, ibid., p. 186.

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Volume 16 | January, 1961 | Number 1

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SCIENTIFIC ARTICLES

Chlordiazepoxide (Librium) in the Treatment of Strabismus; a Preliminary Report, *Mary C. Fletcher, M.D.* 37

Cancer of the Skin, *Marga H. Sinclair, M.D.* 45

Recent Advances in Pediatric Tuberculosis, *Katharine H. K. Hsu, M.D.* 52

Some Diagnostic and Therapeutic Problems of the Superficial Mycoses, *Rachel Ford Spiller, M.D.*, and *William Fielding Spiller, M.D.* 56

Respiratory Distress in the Newborn Infant, *Murdina M. Desmond, M.D.* 59

SPECIAL FEATURES

Benjy F. Brooks, M.D., *Guest Editor* 44

Congratulations to Dr. Janet Grame Travell 78

REGULAR FEATURES

President's Message, *Claire F. Ryder, M.D., M.P.H.* 65

Album of Women in Medicine, Goldie Suttle Ham, M.D., *Benjy F. Brooks, M.D.* 67

Opportunities for Women in Medicine 68

News of Women in Medicine 69

Branch News 70

(Continued on Page 7)

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Table of Contents

(Continued from Page 5)

MISCELLANEOUS

Editorial Board 14
Board of Directors 16
State Directors 18
Branch Officers 24

AMWA Junior Membership Blank 24

AMWA Membership Blank 32

Junior Branch Officers 86

Index to Advertisers 87

Index to Products Advertised 87

Information for Contributors

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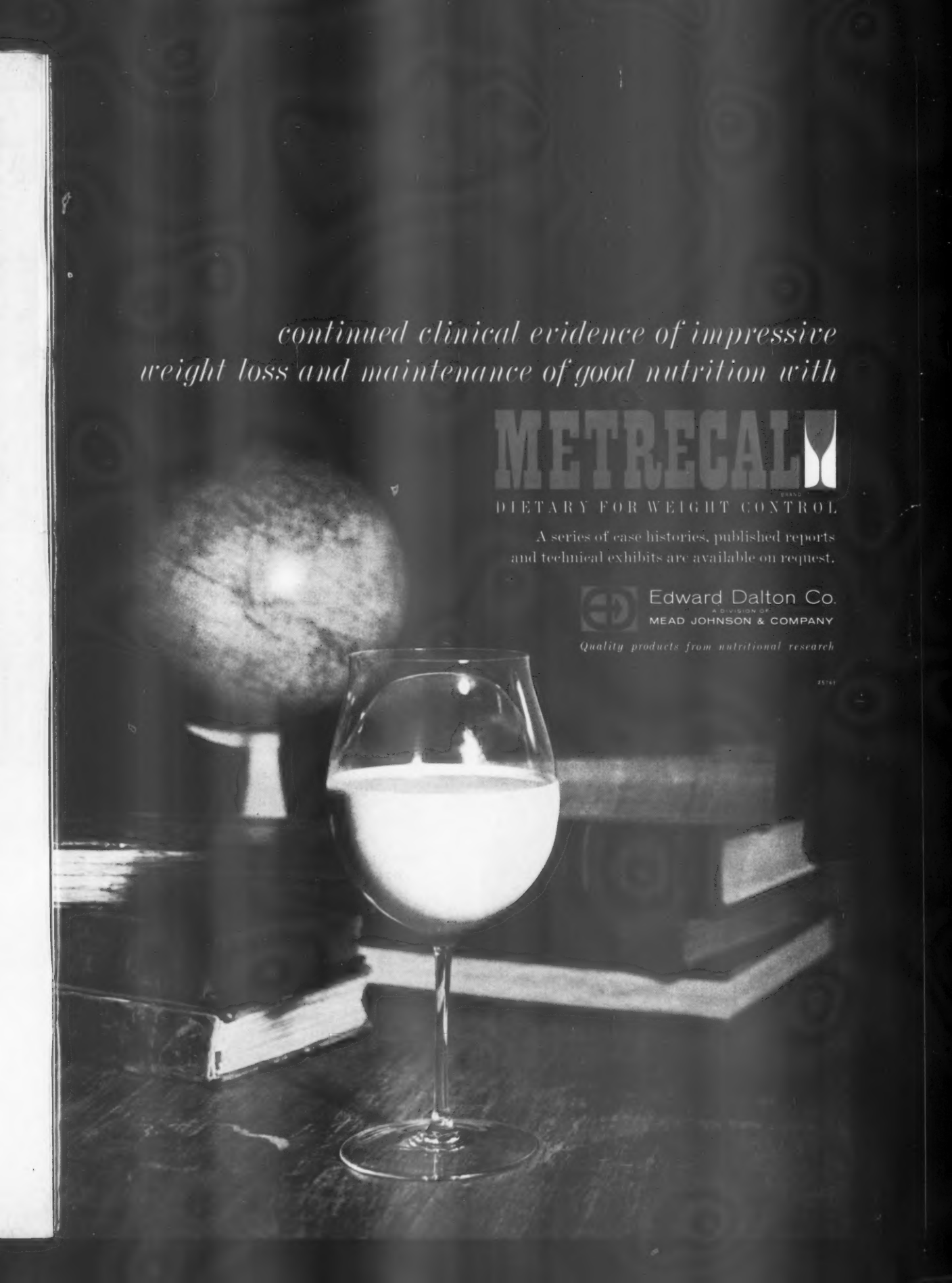
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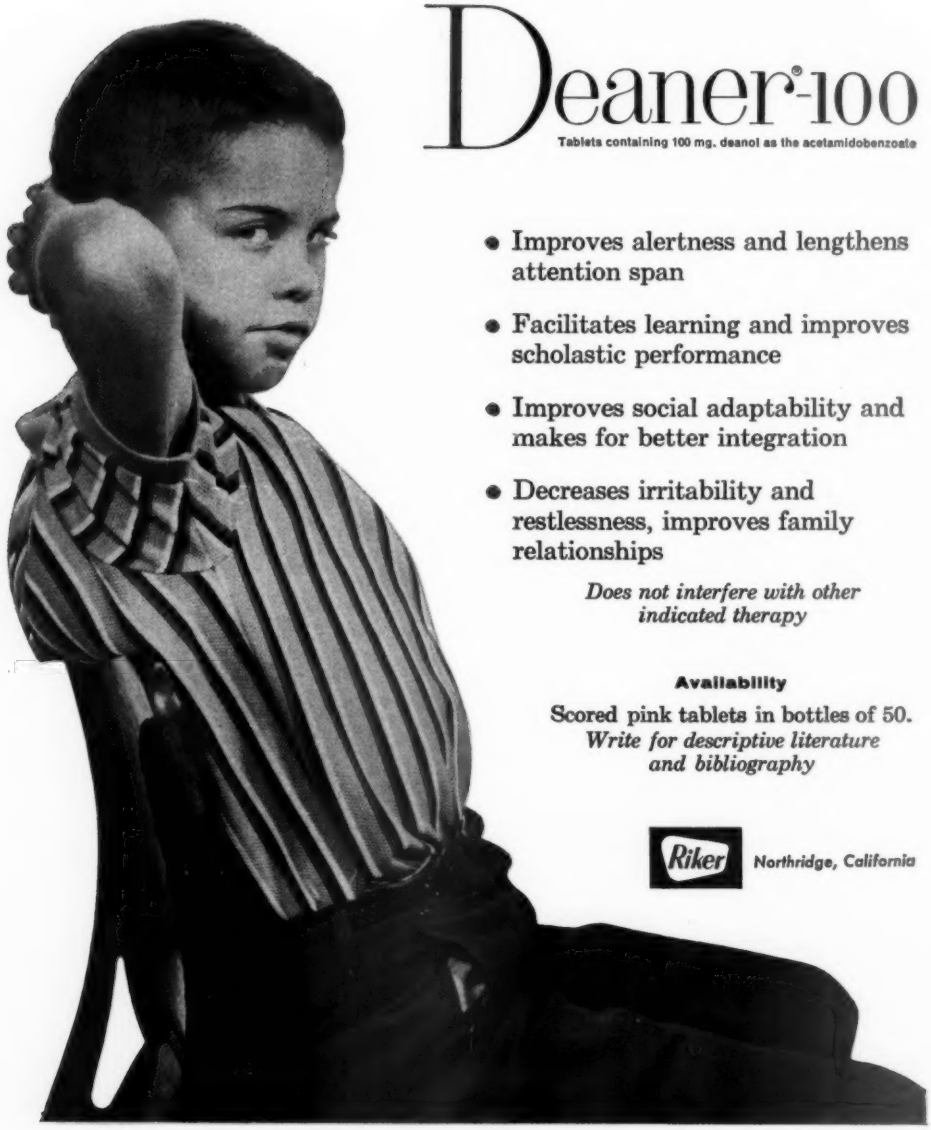

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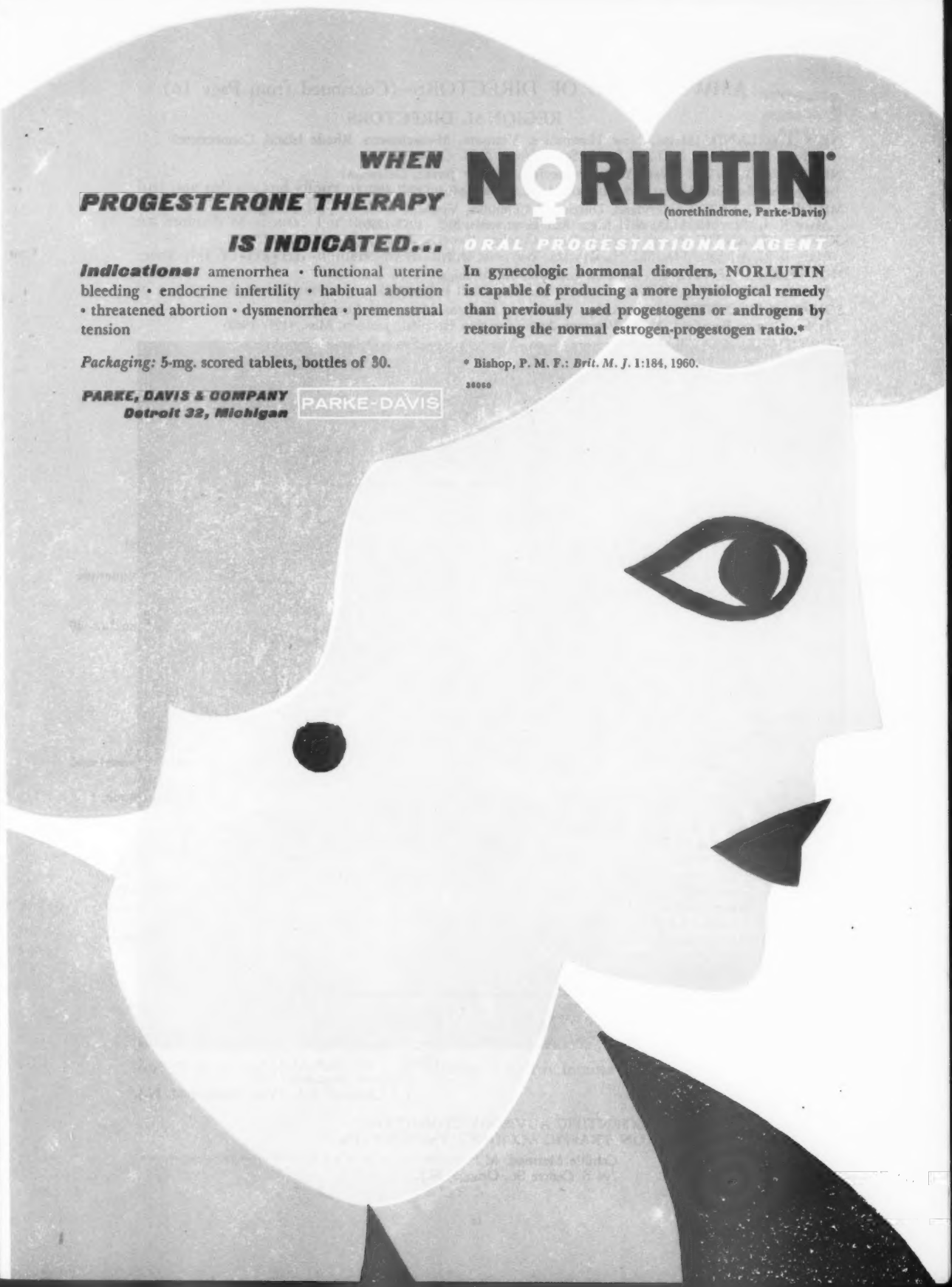

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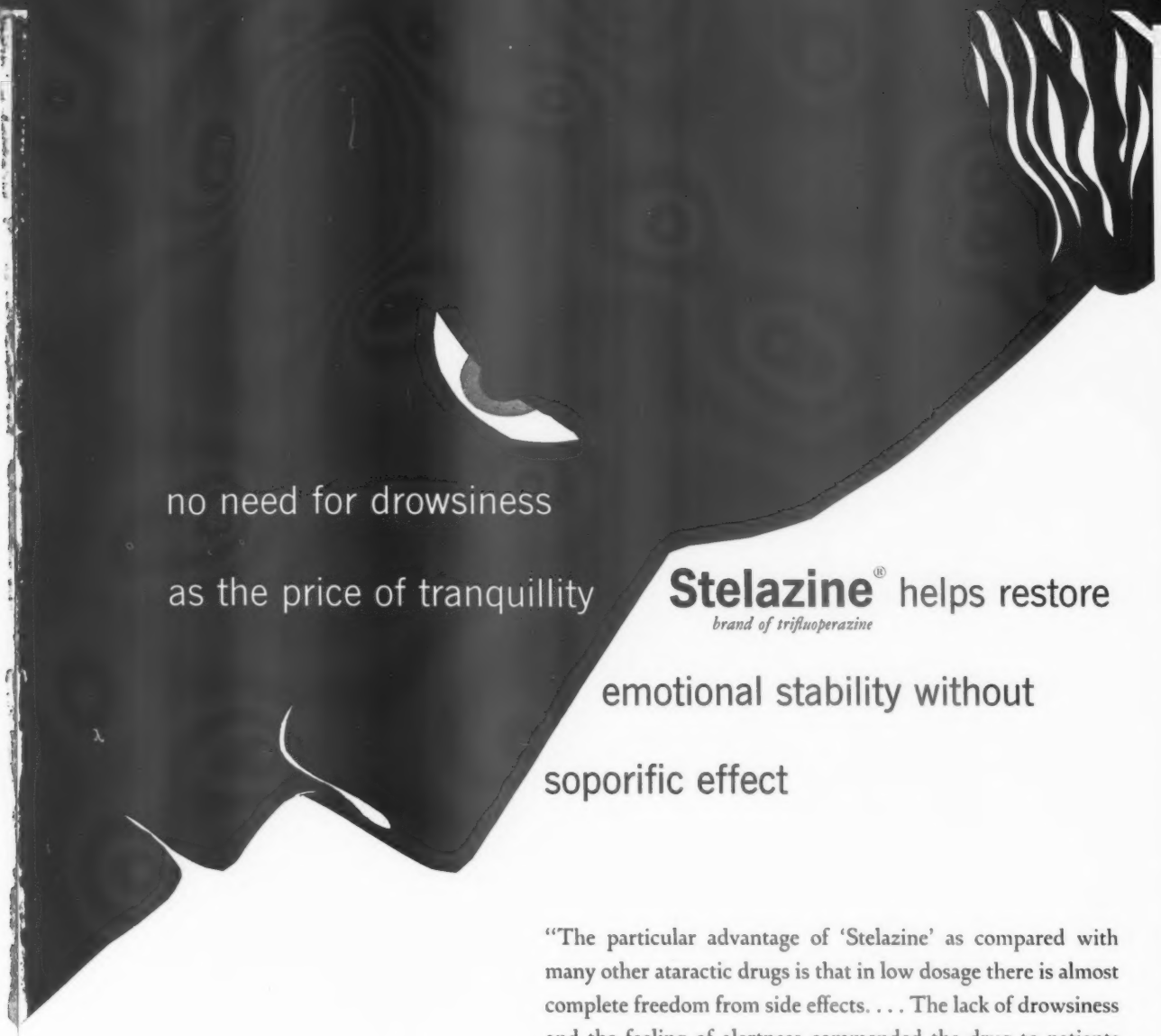

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1. Bram, G.: The Treatment of Psychoneurotic Conditions with Trifluoperazine, Brit. J. Clin. Pract. *14*:107 (Feb.) 1960.

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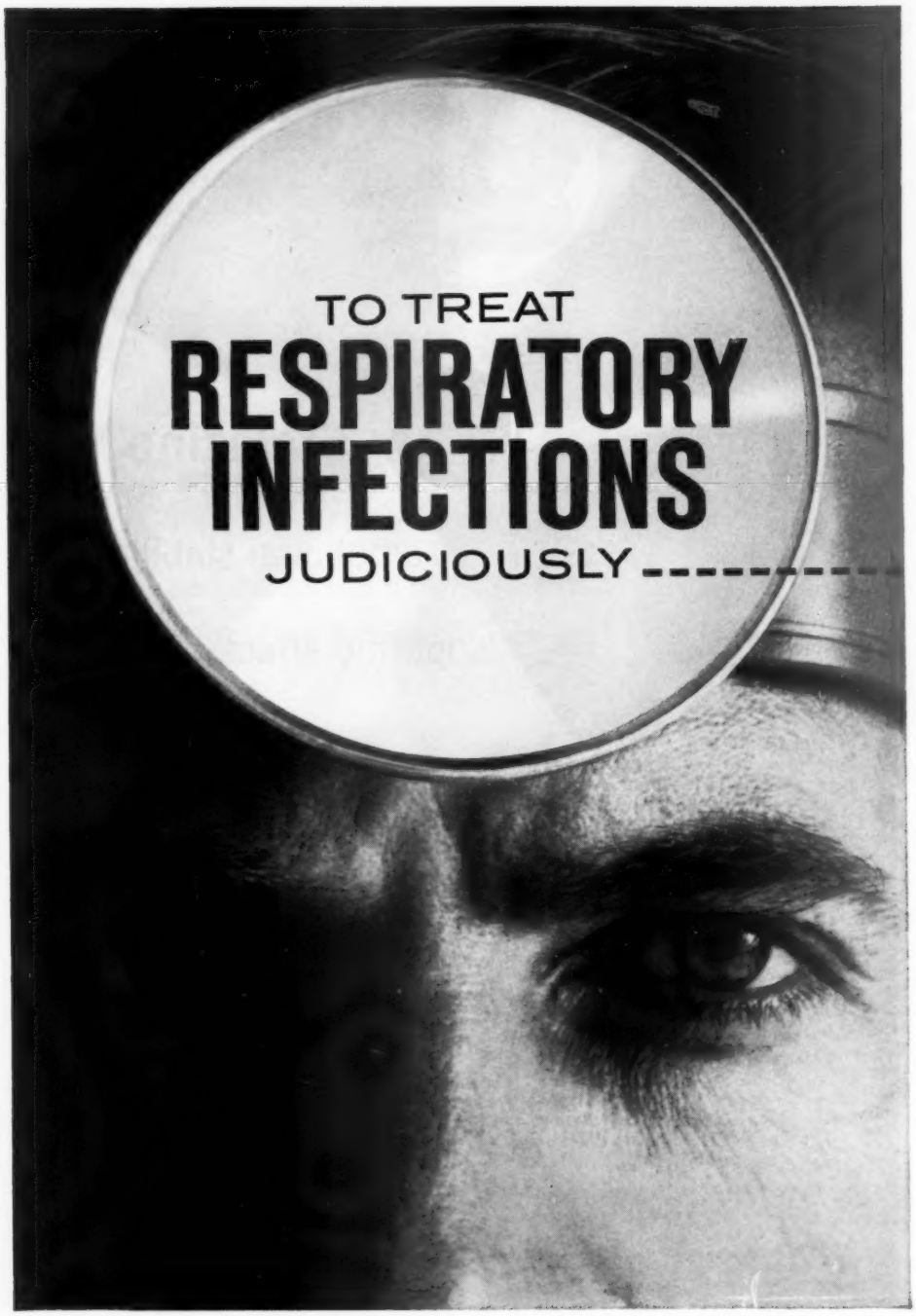
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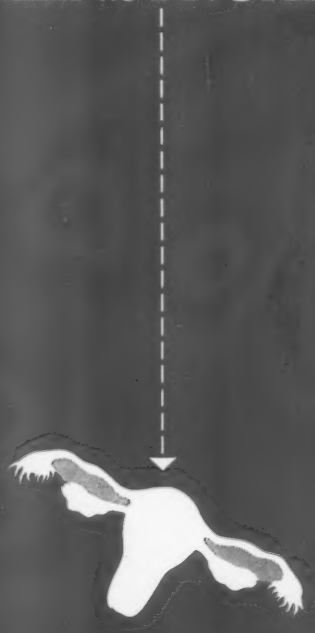

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1. Goodman, L. S., and Gilman, A.: The Pharmacologic Basis of Therapeutics, Second Edition, The Macmillan Company, New York, 1955, pp. 1454-5.

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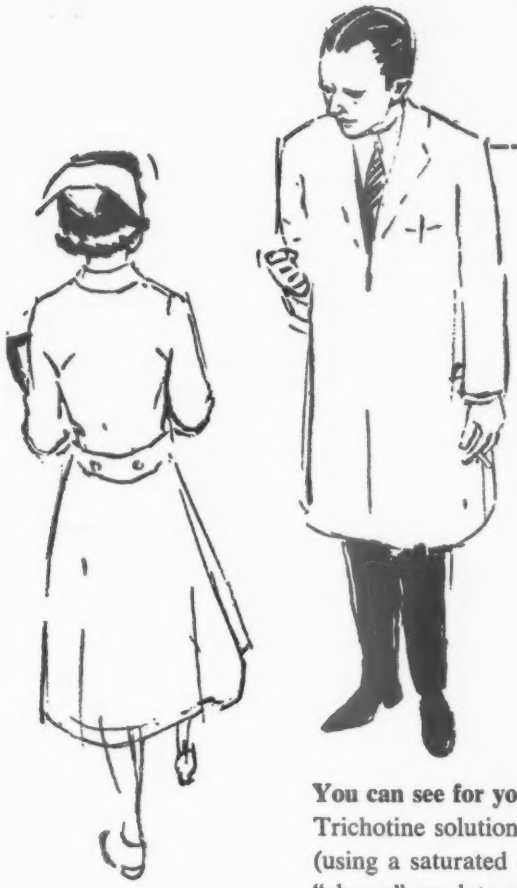

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1. Randall, L. M. 2. Reich, W. J., Rubenstein, M. W., Nechtow, M. J., and Reich, J. B. (literature available on request).

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1. Karnaky, K.J., Tri-State Med. Journal, June, 1960
2. Schaefer, George, Clin. Obst. & Gynec., June, 1959
3. Burrus, Swan, Jr., Am. J. Obst. & Gynec., Aug., 1960
4. Liswood, R., Obst. & Gynec., May, 1959

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Chlordiazepoxide (Librium*) in the Treatment of Strabismus; a Preliminary Report

Mary C. Fletcher, M.D.†

UP TO DATE, drugs have been of little value as an effective nonsurgical means of correcting strabismus. For several years,[1] we have been investigating potential adjuncts to the treatment of squint, and have had indifferent results with the use of drugs belonging to the sedative, tranquilizing, anticonvulsant, and muscle relaxant groups.

Krimsky[2] reports some success with the administration of atropine and pilocarpine; Guibor[3] advocates the use of atropine alone for esotropia and convergence excess. In children 6 years old and older, Costenbader[4] has found "considerable satisfaction" with cyclopentolate (Cyclogyl) hydrochloride with or without homatropine.

* Trademark of Hoffman-La Roche, Inc., Nutley, N.J.

†With the assistance of Mrs. Barbara A. Smith.

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The most encouraging results in the treatment of esotropia have been obtained, however, by the use of DFP (isofluorophate) and it is this drug that we have used routinely. Costenbader[5] has reported the use of DFP in more than 300 patients seen in his office; he explains the rationale for the use of miotics as follows: ". . . since accommodative effort (which must be mediated by the central nervous system) induces convergence, the use of a drug which accomplishes accommodation peripherally or with less central effort would allow for less accommodative convergence." His premise is pertinent to the use of the new compound chlordiazepoxide (Librium), for this, too, acts upon the central nervous system. Costenbader[5] administered tranquilizing drugs to patients with hyperkinetic esotropia and he stated that "they offer some hope for improvement."

Miller[6] recently tried three other cholinesterase inhibitors in 38 patients with accommodative esotropia. He used echothiophate iodide, demecarium bromide and a German drug, Mintacol. In a comparative study with DFP, he found these compounds equally

TABLE I
Improvement in Patients Treated with Chlordiazepoxide (Uncontrolled Study)

Strabismus Type	Improvement	No Improvement	Worse	Total
Esophoria-tropia	14	19	0	33
Exophoria-tropia	1	3	0	4
Hyperphoria-tropia	0	2	0	2
Total	15	24	0	39

effective, with the added advantage that there were no such side effects as are often produced by DFP, namely, iris cysts, severe headache, and keratitis. In addition, Miller found the water-soluble factor in these newer drugs a great advantage. In his experience, he found that patients develop tolerance to all miotics after prolonged use, and a change of medicaments often brings about a fresh cycle of improvement.

Our initial experience with the use of chlordiazepoxide was in a patient with very early intermittent exotropia who, after 6 months of chlordiazepoxide therapy alone, now has a comfortable exophoria. The results in this present study are best in the esophoria-tropia and esotropia groups. Only one patient with a purely accommodative esotropia has been studied to date; this is an adult who was placed on chlordiazepoxide for cosmetic purposes. She became esophoric without correction on 40 mg. daily.

Since the preliminary reports on the use of chlordiazepoxide seemed to indicate the possibility of its effectiveness in a wide area, and because of the rather surprising result of its efficacy in our case, a double-blind study of its effect on a selected group of 100 patients with strabismus was undertaken. The results thus far are of such interest that they warrant a report on the first 51 cases. An additional 39 patients have been observed but not studied in detail (Table I).

MATERIAL AND METHODS

The patients selected for treatment had a heterotropia or heterophoria-tropia; those with heterophoria were excluded. Costenbader's[5] classification has been used with few exceptions. Progressive childhood esotropia with onset at from 6 months to 3 years, is the most common type of strabismus; it worsens progressively over a period of months or years, resulting in a constant large esotropia. These are largely incomitant, associated with a varying degree of vertical anomaly. This one category comprises the individual classifications as used by Costenbader, namely, mixed accommodative and nonaccommodative, comitant tonic acquired, comitant mechanical, and incomitant paretic esotropias. Those patients designated as hypoaccommodative have residual nonaccommodative esotropia but show no signs of progression.

TABLE II
Maintenance Dose of Chlordiazepoxide

	No. of Patients	Mg./Kg.
	4	0.5
	3	0.75
	5	1
	4	1.25
	4	1.5
	17	1.75
	14	2
Total	51	

In the experimental group there were 39 patients with esophoria-tropia, 6 with exophoria-tropia, and 6 with hyperphoria-tropia. All of the patients possessed potentially normal sensory mechanisms, that is, the condition of those under the age of 3 years was alternating, with presumed equal vision and normal ability to fuse. All patients over 3 years of age exhibited equal vision with amblyoscopic evidence of fusion, grade I and/or II, at their objective angle, and at least 5 prism diopters of amplitudes. We felt that these criteria were necessary, in strabismus, to establish measurable effects of drug therapy directed toward the central nervous system.

Of the 51 patients, there were 20 boys and 31 girls. Their ages ranged from 10 months to 11 years, with an average age of 5 years.

Many of the patients had had previous treatment with surgery, orthoptics, pleoptics, DFP, and/or eyeglasses. Excluded from the study were those patients who showed evidence of recent improvement. All existing treatment was continued throughout the experiment with the exception of orthoptics; muscle exercises were discontinued.

The children selected for treatment with chlordiazepoxide were put into two groups alternately. Their placement and medication were known only to the one who controlled the study. The patients in group "A" were given chlordiazepoxide for 4 weeks, then a

TABLE III
Improvement in Patients Treated with Chlordiazepoxide (Controlled Study)*

Strabismus Type	Improvement	No Improvement	Worse	Total
Esophoria-tropia	18	21	0	39
Exophoria-tropia	0	5	1**	6
Hyperphoria-tropia	0	6	0	6
Total	18	32	1	51

* Half of the time during the study each patient received a placebo, and none showed improvement during this period.
** See text.

placebo for 4 weeks. Those in group "B" were given a placebo for 4 weeks, followed by chlordiazepoxide for 4 weeks. Since the status of each patient was known before and after treatment, each served as his own control. All of the children were examined by an ophthalmologist and an orthoptic technician prior to treatment and weekly thereafter during the eight week course, and their records were kept separately. No information was divulged until the end of the eight week period, at which time each case was evaluated. To reach a composite or average picture of results, the measurements taken by the ophthalmologist and the orthoptist were combined. If disagreement existed, the measurements taken were considered inaccurate and that case was rated a failure.

Chlordiazepoxide was given in divided doses three times daily, beginning with 1 mg./Kg. and increasing to 2 mg./Kg. If side effects occurred, the dosage was then reduced by 5 mg. or 10 mg. and administered for the prescribed period. The distribution of the dosage is shown in table II.

The criteria selected to denote improvement in these patients were: (1) determination of their phoria and tropia status by cover test; (2) objective measurement of this deviation by prism and cover, expressed in prism diopters; (3) objective and subjective measurement of their convergence and divergence amplitudes, using the prism bar—all of these amplitudes are given from zero (relative convergence and divergence); (4) objective and subjective measurement of their deviation on the amblyoscope—all patients were required to have identical objective and subjective angles; and (5) convergence and divergence amplitudes on the amblyoscope, indicated from their angle of deviation (total convergence and divergence).

TABLE IV
Improvement in Types of Esophoria-Tropia

	Improvement	No Improvement	Total
Progressive Childhood Esotropia	9	9	18
Hypoaccommodative	5	5	10
Congenital	2	3	5
Old Esotropia	1*	2	3
Hyperkinetic	0	2	2
Convergence Excess	1	0	1
Total	18	21	39

* See text.

RESULTS

There was a definite improvement in the strabismus in 18 of the 51 patients under chlordiazepoxide therapy. They all were in the group of 39 patients with esophoria-tropia and esotropia. The improvement rate for this type of strabismus was, therefore, 46 per cent (Table III).

In group A, in which the patients received chlordiazepoxide for the first four week period, there was some carry over of improvement lasting one to two weeks into the second four week period when a placebo was administered. There was no essential variation in the weekly measurements of the children in group B—who were given a placebo for the first four week period. In all but three patients, the maximal improvement was noted after one week on chlordiazepoxide. Of these three, one showed maximal improvement at two weeks; another, at three weeks; and the third child, although having shown maximal improvement at one week, was rated as unimproved because the improvement subsequently decreased.

TABLE V
Types of Improvement in Esophoria-Tropia with Chlordiazepoxide

Improvement in Prism and Cover (Prism Diopter)*	Improvement in Fusional Amplitudes	No Improvement in Fusion	Total
5-10	2	5	7
10-15	4	2	6
15-20	5	0	5
>20	0	0	0
Total	11	7	18

* An additional 5 patients showed improvement in prism and cover measurements but the ophthalmologist and the orthoptist disagreed, and these cases were discarded.

TABLE VI
Improvement on Chlordiazepoxide

Cl. #		Before Chlordiazepoxide		On Chlordiazepoxide		After Chlordiazepoxide	
		P & C	Amblyoscope	P & C	Amblyoscope	P & C	Amblyoscope
1	Progressive Childhood Esotropia 2763 F 3 yrs.	SC E-14 D-0 E-ET′-18 D′-0	SC E-18 C-12 D-10 (obj.)	SC E-0 D-4 E′-0 D′-10	SC E-0 C-30 D-15	ET-20 C-0 ET′-30 D′-0	ET-20 C-10 D-10
2	Old Esotropia 1411 F 7½ yrs.	CC E-ET-12 D-0 E-ET′-25 D′-0	CC E-25 C-15 D-30	CC E-0 C-8 D-2 E′-0 C′-20 D′-6	CC E-0 C-30 D-15	E-ET-14 C-4 D-1 ET′-18 C′-0 D′-0	E-20 C-18 D-22
3	Progressive Childhood Esotropia 1295 F 5 yrs.	CC ET-12 RH 14 LH 2 C&D-0 ET′-12 RH 14 LH 1 C′&D′-0	CC E-20 RH 10 C-6 D-4	CC E-4 RH 6 LH 2 E′-10 RH 4 LH 1	CC E-10 RH 2 C-20 D-14	CC ET-12 RH 8 D-0 E-ET′-14 RH 6 D′-0	CC E-14 RH 4 C-10 D-8
4	Hypoaccommodative 2783 F 3½ yrs.	CC E-6 C-20 D-2 E-ET′-10 C′-0 D′-0	SC E-30 C-25 D-20 ? Accommodating on instrument	CC E-0 D-1 E′-2 D′-14	CC E-8 C-22 D-18	Was kept on chlordiazepoxide because 1 week after withdrawal, child became so irritable parents requested she be placed back on drug.	
5	Convergence Excess Nonaccom. 1435 M 9½ yrs.	SC E-0 C-8 D-1 E-ET′ 10 C′-0 D′-0	Missed	SC E-2 D-2 E′-0 D′-12	SC E-5 C-20 D-8	SC E-0 C-6 D-4 E-ET′-8 C′-10 D′-0	SC E-10 C-15 D-12
6	Strabismus Fixus, Post-surgery 2337 F 10 mos.	SC E-ET 30 E-ET′-30	– – – –	SC E-ET-8 E-ET′-8	– – – – –	Chlordiazepoxide continued. With addition of DFP (previously of no help) she is fusing all day long.	
7	Progressive Childhood Esotropia 2889 M 5 yrs.	SC E-ET-40 C-4 D-0 E-ET′-40 RH C′-40 D′-0	SC E-55 C-10 D-10 (Accommodating on instrument)	SC E-ET-14 D-6 E-ET′-16 D′-18	SC E-18 C-37 D-22	SC E-ET-35 D-4 E-ET′-35 D′-0 1 week only. Parents refused to continue placebo. Placed back on Chlordiazepoxide.	E-40 C-10 D-10
8	Hypoaccommodative 1315 F 5½ yrs.	CC E-0 D-? E-ET′-12 D′-0 SC ET-20 ET′-25	E 2 C-10 D-10	CC X-2 D-6 X′-2 D′-12 SC E-0 E′-0	CC E-0 C-25 D-10	CC E-ET-8 C-6 D-2 E-ET′-14 C′-0 D′-0 After 4 weeks she still did not return to former state.	E-8 C-12 D-10

9	Progressive Childhood Esotropia 117 M 6½ yrs.	CC ET-10 E-ET′-14 C-20 D-10	CC E-8 C-17 D-10	CC E-ET-8 E′-2	CC E-2 C-28 D-12	CC ET-10 D-0 ET′-10 D′-0	CC E-8 C-15 D-12
10	Hypoaccommodative 2280 F 5 yrs.	CC E-12 D-4 E-ET′-14 D-0	CC E-10 C-20 D-8	CC E-2 C-10 D-4 E′-8 C′-30 D′-6	CC E-4 C-26 D-12	CC E-10 C-8 D-0 E-ET′-14 C′-20 D-0	CC E-10 C-15 D-5
11	Progressive Childhood Esotropia 1476 F 4 yrs.	CC E-ET-10 C-0 D-0 E-ET′-12 C′-40 D′-0 SC ET-16 ET′-16	CC E-8 C-20 D-12	CC E-0 C-10 D-4 E′-0 C′-35 D′-14 SC E-0 E′-2	CC E-0 C-20 D-10	CC E-6 C-2 D-1 E-ET′-12 D-0 SC ET-14 D-0 ET′-16 D′-0	CC E-5 C-20 D-10
12*	Progressive Childhood Esotropia 1681 F 3½ yrs.	CC ET-20 ET′-15 SC ET-30 ET′-25	E-25 C-20 D-10	CC ET-10 ET′-12 SC ET-16 ET′-18	E-10 C-20 D-12	CC ET-18 ET′-20 SC ET-30 ET′-25	E-25 C-15 D-10
13*	Progressive Childhood Esotropia 2127 F 2 yrs.	CC ET-18 ET′-25 Bifocal ET′-20 SC ET-35 ET′-35	– – – – –	CC ET-10 ET′-8 Bifocal ET′-10 SC ET-25 ET′-25	– – – – –	CC ET-18 ET′-22 Bifocal ET′-18 SC ET-30 ET′-35	– – – – –
14*	Progressive Childhood Esotropia 2629 F 2 yrs.	CC ET-35 ET′-30 SC ET-50 ET′-45	E-38 (Subj.)/C-12 D-23 (Obj.)	CC ET-14 ET′-16 SC ET-20 ET′-20	E-20 C-10 D-15 (Subj.)	CC ET-25 ET′-25 SC ET-40 ET′-40	– – – – –
15*	Progressive Childhood Esotropia 2367 F 2½ yrs.	CC ET-14 ET′-16 LH	– – – – –	CC E-6 (?)** E-ET′-8 (?)	– – – – –	CC ET-16 RH ET′-16	– – – – –
16*	Hypoaccommodative 837 F 4½ yrs.	CC E-ET-8 ET′-18 Bifocal E-ET′-10(?) SC ET-30 ET′-45	CC E-8 C-12 D-12 Paresis of both Superior Recti 2+ Paresis of both Superior Oblique 3+ (Observed for 2 years)	CC E-ET-4 (?) E-ET′-10 (?)** Bifocal E-4 (?) SC ET-20 ET′-21	CC E-4 C-20 D-14 No paresis of Superior Recti No paresis of Superior Obliques	CC ET-6 ET′-18 Bifocal ET′-14 SC ET-40 ET′-45	– – – – Return of original paresis of superior recti & obliques

17*	Congenital Esotropia	CC LH-18 LH'16	CC LH-13 C-10 D-4	CC X-XT-12 LH-10 E'0 LH-10 Reading XT-14 (Child refused eyeglasses) SC E-ET-10 LH Variable E-ET'10 LH Variable	CC LH-5 C-12 D-6 SC ET-5 LH-5 C-20 D-15	SC ET-18 LH-12 ET'-18 LH-10	SC ET-18 LH-9 C-12 D-8
‡	143 F 4 yrs.	SC ET-14 LH-10 ET'12 LH'10					
18*	Hypoaccommodative	CC E-12 C-12 D-2 E-ET'14 D'2	CC ET-18 C-25 D-17	CC E-ET-10 D-2 E-ET'10 D'14 SC ET-20 ET'20	CC ET-12 C-15 D-10	CC E-ET-12 E-ET'12	– – – –
‡	1458 F 3½ yrs.	SC ET-35 ET'25					

* Improvement in Prism and Cover Measurements Only.
** Disagreement on fusion.
* Variable measurements but agreement on Improvement.

Key: SC-Without eyeglasses
CC-With eyeglasses
E-Esophoria at distance (20 ft.)
E'-Esophoria at near
X-Exophoria
ET-Esotropia at distance (20 ft.)
ET'-Esotropia at near
C-Amplitude of convergence in prism diopters
D-Amplitude of divergence in prism diopters

Thirty-two of the patients were judged as unimproved. One patient with a primary intermittent exotropia with secondary convergence insufficiency was considered as worsened by chlordiazepoxide treatment. During her four weeks on chlordiazepoxide she lost her convergence amplitudes and developed a frank exotropia, both distance and near. When chlordiazepoxide was discontinued, she again showed an intermittent exotropia.

The esophoria-tropia type of strabismus thus far has proven to be the most amenable to drug therapy (Table III). Table IV shows the response of this group by diagnostic categories. The single case of "old esotropia" (which improved under chlordiazepoxide therapy), was a 7½ year old girl, who was first seen by us 1½ years ago. She had had alternating esotropia of 70 prism diopters distance and near. After resection of the lateral and retroplacement of the medial recti of the left eye, she still had a partially accommodative esophoria-tropia. Prior to chlordiazepoxide therapy, orthoptic exercises had been given for 5 months, with no improvement after the first 3 months. After two weeks on chlordiazepoxide, she became orthophoric with eyeglasses, and increased her amplitudes of fusion spontaneously (Table VI, case 2).

Table V shows the improvement noted in the 18 patients, correlating their degree of prism and cover improvement and improvement in fusional amplitudes. There was a correlation between degree of horizontal improvement and improvement in fusional amplitude. Eleven patients gained in both functions while 7 improved only in prism and cover measurements.

A detailed report of each of the 18 patients who benefited from the use of chlordiazepoxide is presented in table VI. The scope and functions of this drug cannot be based definitively on the results obtained in so small a group, but various indications are worthy of note. Case 7, a 10 month old girl, who was operated on for strabismus fixus at 5 months of age, had been receiving DFP without benefit before our study began. After the eight week period, both chlordiazepoxide and DFP were administered and the eyes are fusing continuously. A dramatic effect of the drug was noted in case 16; this was a 4½ year old girl who had been under observation for 2 years. She had paresis of both the superior recti and superior oblique muscles; this

disappeared when chlordiazepoxide was administered and recurred when the drug was discontinued.

Several of the patients, or their families, gave distinct evidence of their liking for chlordiazepoxide. When it was replaced by a placebo in a 5 year old boy with progressive childhood esotropia, his parents refused to continue the placebo and he was put back on chlordiazepoxide (Case 7). A girl of 3½ years with hypoaccommodative esotropia became so irritable a week after withdrawal of chlordiazepoxide, her parents requested that she be given the drug again (Case 4).

Thirty-seven of the 51 patients developed side effects when given 2 mg./Kg. of chlordiazepoxide; 14 of these patients continued to have mild side effects even after the dosage was decreased, but their symptoms did not warrant the discontinuance of the drug. The average maintenance dose was approximately 1¾ mg./Kg. Fourteen patients showed side reactions to this dosage; 10 displayed irritability and 4, drowsiness. Thus far, only six of the children have been completely unable to tolerate chlordiazepoxide; one had temper tantrums; two developed a skin rash; two became agitated; and the sixth child was depressed. When bed wetting had been present, it seemed to stop; occasionally, it had its onset during the administration of the drug.

DISCUSSION

No assessment of the role of the use of chlordiazepoxide in the treatment of strabismus is possible at this time because of the small group involved in this progress report and because of the complexities of the condition and the still unknown area of action of chlordiazepoxide. It can only be stated categorically that this is the most effective drug thus far used by us as a chemotherapeutic adjunct in the correction of strabismus. The analysis of prism and cover improvement and gains in fusional amplitudes suggest that there is a definite correlation between the degree of improvement in horizontal deviation and the improvement in fusional amplitudes. In our opinion, the latter gain was not directly related to the drug but rather to the fact that since the horizontal deviation was less, casual fusion was made possible, and this resulted in increased amplitudes.

We have the impression that we are not influencing heterotropias by the tranquilizing or sedative effect of the drug. Most of the children had no noticeable drug effect when on their therapeutic dosages. Two were irritable and two were depressed. The double-blind study was carefully conducted so that suggestion could hardly have played any role to the parents, the children, or the examiners. These facts lead us to believe that the mode of action is on either the convergence, divergence, accommodative-convergence, or the fusion centers in the central nervous system. Peripheral action on the myoneural junction or on the eye muscles themselves is, of course, a possibility, but less likely.

There are inadequate data in this study to identify the site of action. The worsening of intermittent exotropia suggests relaxation of convergence and possibly accommodation or the stimulation of divergence. The improvement of one such patient, if this can be substantiated, suggests relaxation of divergence or stimulation of convergence or accommodation. The improvement in patients with esotropias suggests stimulation of divergence or relaxation of convergence or accommodation. Data are insufficient to support a thesis that an altered accommodation or accommodative-convergence ratio exists. These data are impossible to obtain accurately in the infant and the child. The case of the adult which we have cited suggests that this mechanism may be involved.

The failure of chlordiazepoxide to produce a predictable, measurable, and an all-or-none response in children with strabismus is disappointing, but we think understandable. Most of our drugs acting on the central nervous system have the same drawback. It behooves us to explore allied drugs, especially those that may alter the difficult vertical problems.

SUMMARY

In a double-blind study, 51 patients with strabismus were treated with a new drug, chlordiazepoxide (Librium). Eighteen patients definitely benefited from therapy. All the children who showed improvement had the esotropia or esophoria-tropia type of strabismus; other types did not respond.

The results suggest that a new and important medicament is available for use in the treatment of strabismus.

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BENJY F. BROOKS, M.D.

Guest Editor

Conviction and enthusiasm are two requisites for the successful practice of medicine. Persons with these attributes bridge the gap between the humanism of kindly medical practitioners and the materialism of impersonal doctors. One of the representatives of a generation of physicians epitomizing humanism in medicine is the guest editor for this issue, Dr. Benjy F. Brooks.

Dr. Brooks practices pediatric surgery and carries out experimental surgical research. In addition, she holds clinical faculty appointments at Baylor University of Medicine and the University of Texas Postgraduate School of Medicine. She is a Diplomate of the American Board of Pediatrics and American Board of Surgery; a Fellow in the American Academy of Pediatrics and American College of Surgeons, and is President of the Houston branch of the AMWA.

Dr. Brooks graduated from North Texas State College and received her M.D. degree from the University of Texas School of Medicine. She interned at the Woman's College Hospital in Philadelphia and was a resident in pediatrics there. Residency training in surgery was secured in Philadelphia at the University of Pennsylvania Graduate Hospital and Veterans Administration hospital. She was a resident in pediatrics in Boston at the Children's Medical Center, where she was the first woman honored by being accepted for training in pediatric surgery by Dr. Robert Gross at Harvard University.

Child health has also claimed Dr. Brooks' interest abroad. The North Atlantic Region of the American Federation of Soroptimists' Clubs awarded her a traveling fellowship, and for 12 months, in Glasgow, Scotland, Dr. Brooks held the position of Registrar in Children's Surgery at the Royal Hospital for Sick Children. The city of Glasgow named her "Chosen Woman of The Year," an honor doubtless recording the esteem held for her by those Scots capable of judging people blessed with sane forthrightness and straight thinking.

Dr. Brooks is a cosmopolitan person and a befriender of young patients, parents, nurses, students, and resident physicians. But she also is a provocateur; she has things to say. And she puts honesty and truth at the center of her life.

—Fred M. Taylor, M.D.

Cancer of the Skin

Marga H. Sinclair, M.D.

CANCER OF THE SKIN is a serious problem in some parts of the world, including the southern United States. Skin cancer comprises 35 per cent of all cancer in Texas, more than 50 per cent in Australia, only about 5 per cent in England and 3 per cent in Bombay, India. Reports of Allison and Wong[1] show that in Honolulu skin cancer is 45 times as common among Caucasians as among non-Caucasians. More than 80 per cent of all skin cancers appear on the uncovered areas of the body. These statistics indicate that prolonged exposure to sunshine plays an important part in the etiology of skin cancer and, further, that the fair-skinned races are more susceptible than are those with darkly pigmented skin.

A comparative study of the incidence of skin cancer in the state of Connecticut and El Paso County, Texas, based on the State Cancer Record Registries of both areas, was made by Eleanor Macdonald,[2] Epidemiologist of the M. D. Anderson Hospital. There is a decided contrast in the climate of the two areas. El Paso lies high; it is dry, windy, and hot, and the sun shines 80 per cent of the possible daylight hours. Connecticut is low, less windy, and humid. It has a low mean temperature and the sun shines during only 59 per cent of the possible daylight hours. The study covers a 12 year period. During this period approximately the same number of skin cancers was recorded in El Paso as in Connecticut, although the El Paso population is one eighth as large. Thus, skin cancer was eight times as frequent in El Paso as in Connecticut. In El Paso, most of the skin cancers were located on the face and on the usually exposed areas of the neck, hands, and forearms.

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Multiple lesions were present in 16.3 per cent of the patients. Of those with multiple lesions, 27.7 per cent were of Scottish-Irish descent, persons who are known and reported in other series as especially susceptible to skin cancers because of their fair skin. About 50 per cent of the population of El Paso is Latin-American. In the studies of the Texas Cancer Record Registry, the Anglo-American and the Latin-American groups were considered separately. Skin cancer of the head and neck region comprises 35.8 per cent of all cancer among the Anglo-Americans in El Paso and 8.3 per cent among the Latin-Americans. By way of comparison, the figure was only 7 per cent for all Connecticut residents.

According to the El Paso study, 80 per cent of all the skin lesions of the head and neck region occur on the forehead, the temple, the cheek, the nose, and the upper lip among the Anglo-Americans; 7.9 per cent on the ear, 6.3 per cent on the neck, 3.2 per cent on the outer canthus of the eye, and 1.5 per cent on the inner canthus. Only 1 per cent of the total skin lesions appear on the scalp, probably because outdoor workers in Texas protect their scalps with large hats most of the time.

Belisario[3] of Sydney, Australia, has published interesting statistics about the incidence of skin cancer in Australia which also illustrate the etiologic significance of the number of sunlight hours in the frequency of skin cancer and the greater susceptibility of the white races as compared with the darkly pigmented ones.

Skin cancer, in general, is a disease of later life; it occurs usually in the fourth, fifth, and sixth decades, although it may occur in adolescents and even in children. Skin cancer may arise in apparently normal skin, but it frequently originates from previously altered epidermis. Clinical experience and statistics indicate that low actinic tolerance on exposure to sun and wind, as commonly found in people with fair complexion, is a predispos-

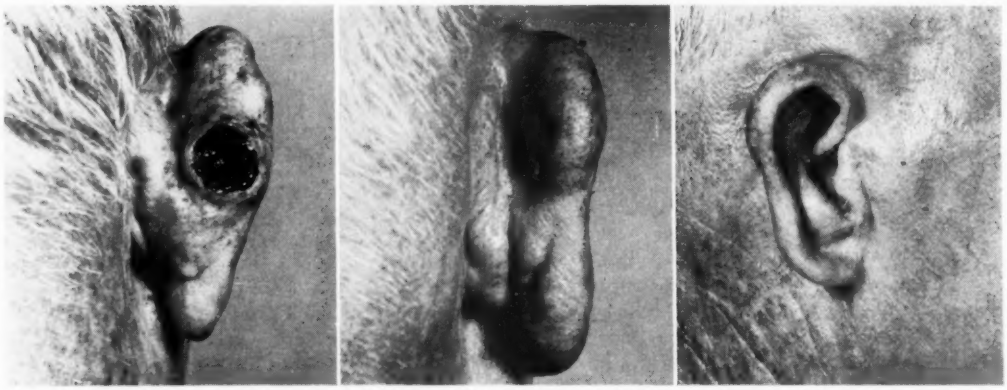

Fig. 1. *(Left)* Squamous cell carcinoma of posterior surface of right ear. *(Center)* After v-excision and repair. *(Right)* After v-excision and repair.

ing factor. The most common precursors of cutaneous cancer are senile or solar keratoses; these occur mostly on the normally exposed areas. However, many senile keratoses may show no malignant changes for many years or may never become malignant at all. Senile atrophy of the skin develops progressively in all individuals during advancing years. The skin becomes dry and thin, it loses its elasticity, and its color becomes grayish pale. Hyperpigmented spots or depigmented areas appear; scaling and telangiectasias may be present. Senile keratoses develop frequently in this type of skin. The individual lesions of senile keratoses are well circumscribed, flat or raised, often wart-like, dark grey or brown, and covered with dry, adherent scales. After the scales are removed, a well circumscribed, bleeding erosion is seen. Senile keratoses develop slowly, then become larger and more numerous. The appearance of inflammatory changes, ulceration, and enlargement should arouse the suspicion that malignant changes have taken place. Usually, squamous cell carcinomas develop from senile keratoses. Often, diagnosis of the malignant change can be made only after histologic examination. Ormsby and Montgomery[4] report that malignant changes occur in one or more lesions in 20 to 25 per cent of patients with senile keratoses.

Other precancerous conditions are arsenical keratoses, which appear commonly on the palms and the soles; industrial keratoses, caused by contact with certain oils of coal tar, anthracene, creosote, and aniline dyes, which appear on the hands, the forearms, and occasionally on the face; and still another precancerous condition is the cutaneous horn. These are circumscribed keratoses which may arise in apparently normal skin, but frequently develop from senile keratoses. They are found mainly on the ears, the nose, the lips, the forehead, and the extremities, but they can also be found on the trunk and on the penis. Cutaneous horns vary in size and form. Although the horny part may fall off, the lesion may keep on growing. About 20 per cent are reported to show malignant changes in the base.

These precancerous conditions do not show any clinical or histologic signs of a malignant growth; the term indicates only that cancer may develop more frequently in them than in other dermatoses or in apparently normal skin.

The principal types of cancer which occur in the skin are (a) basal cell carcinoma, (b) squamous cell carcinoma, and (c) intraepidermal squamous cell carcinoma or "Bowen's disease." Cancer of the skin appendages, originating from sebaceous or sweat glands or from hair follicles are much less frequent.

Basal Cell Carcinoma. The clinical picture and the growth pattern of basal cell carcinoma vary greatly. In some instances, only histologic examination can determine the type of local growth. Knowledge of this local growth pattern, however, is the basis for adequate treatment. We know five different patterns of growth.

1. The nodular basal cell carcinoma is usually the least aggressive. The tumor may remain as a distinct nodule for many years and can be mistaken for a fibroma, but it may also be the early stage of an invasive ulcerative tumor. It can readily be removed by excision;

Fig. 2. *(Left)* Extensive basal cell carcinoma of right temple, right preauricular area, reaching from outer canthus to root of helix. *(Right)* After excision and repair by split thickness skin graft.

pathologic examination usually shows a well defined margin between the tumor and the uninvolved tissue.

2. The cicatrizing basal cell carcinoma begins as a small nodule or as a scaly patch and grows slowly into a larger plaque with irregular, indefinite borders. The center becomes atrophic; it looks like a scar, and it is sometimes mistaken for one. This tumor is deceptive because it usually extends far beyond the grossly involved area. Histologic check of the margins for complete removal is necessary.

3. The ulcerative and invasive basal cell carcinoma begins as a nodule or a plaque. The center ulcerates early while the nonulcerated edges appear rolled. When this tumor is not treated adequately, it may invade the tissues of the nose, the orbit, the facial bones, and the sinuses.

4. The morphea-like basal cell carcinoma appears as an indurated pale plaque with a smooth surface. It may resemble the cicatrizing type or it may penetrate deeply even into the subcutaneous tissue. Because of this deceptive gross appearance, a check of the margins of the excised specimen is absolutely necessary.

5. Multiple superficial basal cell carcinomas appear as small or large, red, dry, scaly patches with irregular borders; occasionally, they are pigmented. They are usually lesions of the trunk. Microscopically, they appear as many small separate clusters of basal cells growing from the deepest part of the epidermis. The individual cell groups are often considered as multiple foci, but special histologic sections show that some are interconnected. Usually, superficial destruction of the foci is adequate treatment, but when single lesions become invasive they require deep excision.

Squamous Cell Carcinoma. In the beginning, a squamous cell carcinoma arising in normal skin often cannot be distinguished clinically from a basal cell carcinoma. In the advanced stages, we distinguish the ulcerated from the papillary types. The ulcerating type also starts with a papule, which enlarges by forming daughter papules. The center ulcerates early and forms an irregular, deep crater, covered with necrotic tissue. The papillary type grows like a cauliflower, sometimes pedunculated on a broad base. The surface bleeds easily and is covered with crusts and scales. Parts of the tumor may become necrotic and slough off.

Most of the squamous cell carcinomas develop from precancerous lesions in previously altered skin, such as senile keratoses, cutaneous horns, and roentgen ray dermatoses. Invasion and cellular differentiation in the histologic examination indicate an aggressive tumor. These tumors grow faster than do basal cell tumors and, usually, the patient seeks treatment earlier. Squamous cell carcinomas can metastasize, but statistics relative to the frequency of metastases from skin cancer are difficult to evaluate.

Intraepidermal Cancer. The third type of skin cancer is the intraepidermal cancer of which Bowen's disease is the most frequent and best defined clinical and pathologic entity. Bowen's disease appears as a sharply defined, papulosquamous plaque. Multiple papules, covered with yellow, grey, or brown

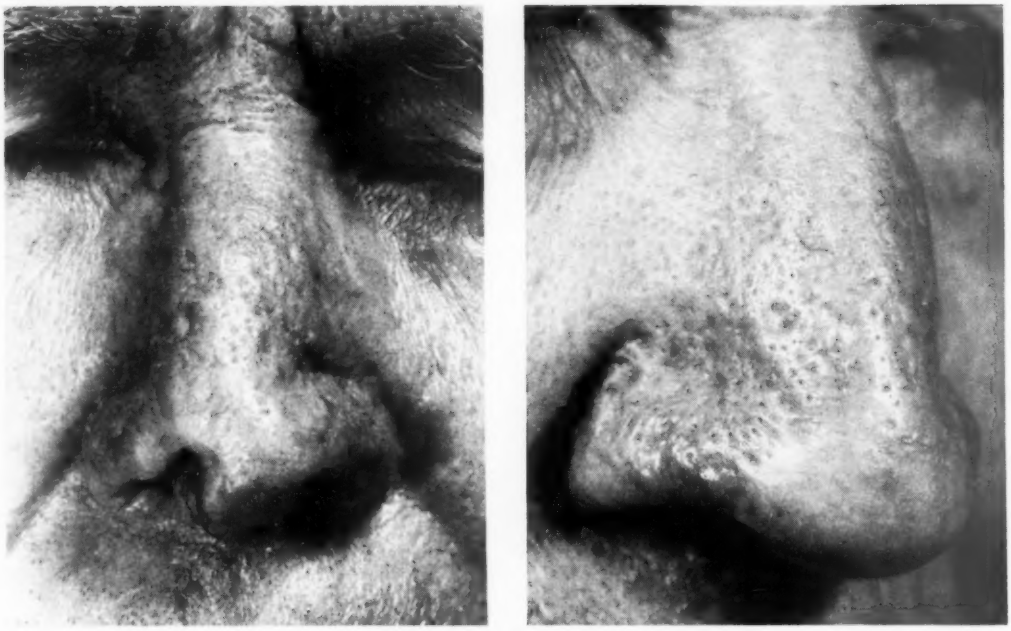

Fig. 3. *(Left)* Defect of right tip and ala of nose after treatment of squamous cell carcinoma by combination of electrocautery and radiation. *(Right)* After repair by composite graft from ear.

scales and crusts usually occur, surrounded by normal or erythematous skin. They may occur as single or multiple skin lesions on any part of the body. Bowen's disease is an intraepidermal squamous cell carcinoma and not a precancerous lesion as it was originally considered. It, too, can metastasize.

Differential diagnosis of basal and squamous cell carcinoma can be very difficult clinically when the lesions are not typical. Biopsy and histologic study are often necessary for definitive diagnosis.

A positive diagnosis is important because basal cell and squamous cell carcinoma run different courses. Basal cell carcinomas usually grow more slowly, but they may invade deeper structures, and even bone, over a long period of time; they may remain unnoticed until they invade a nerve and cause pain. The most dangerous areas in this respect are the nasolabial fold and the inner canthus. Basal cell carcinoma in the skin of the nose may invade the cartilage and the mucosa; this happens frequently when the primary lesion has been treated inadequately by electrocoagulation.

Squamous cell carcinoma usually grows faster and ulcerates more quickly; therefore, the patient comes for treatment earlier. The main danger lies in the fact that it can metastasize and there is no way to know when or why a squamous cell carcinoma will metastasize. The size, the duration, or the location of the primary tumor does not determine the occurrence of metastases. We only know that the regional lymph nodes must be examined carefully at regular intervals to detect the occurrence of metastases as early as possible and to institute treatment.

We have given some thought to the treatment of patients with precancerous lesions. We were impressed by the fact that extensive skin grafts of the face and hands of people whose skin was otherwise covered with senile keratosis stayed smooth for a number of years with adequate care. This was done even though some of these keratoses became malignant while the patients were under our observation. About 3 years ago, we started surgical planing of patients with extensive senile keratoses. Both the immediate and the late results are excellent. All of these patients are much improved; the skin is smooth and no itching areas are present. They have been instructed in the care, and protection from exposure to sun, of this new and tender skin. Even areas on the lateral and posterior neck can be improved by planing.

Fig. 4. *(Left)* Defect of nose after radiation treatment for extensive basal cell carcinoma of the nose and upper left cheek. *(Center)* Lateral view. *(Right)* After reconstruction of nose by forehead flap.

Irrespective of the histologic type of the tumor, local treatment of skin cancer is the same; it is either by surgical excision or by radiation. Diagnosis should be verified by biopsy before treatment is initiated. When it is difficult to judge the extent of the tumor clinically, frozen section examination should be performed at the time of surgery.

In our opinion, radiation treatment should be excluded in all patients with precancerous skin changes and in those with low actinic tolerance. Such skin does not tolerate radiation satisfactorily. In areas with a hot and dry climate, the radiated skin exposed to actinic rays may undergo radiation necrosis and possibly malignant changes. Because of these circumstances, we prefer surgical management of skin lesions for all young people, for all people with light complexion, and for skin cancers of the uncovered areas. In other climates, irradiation in many instances can yield cures with excellent cosmetic results. Certain regions of the body, however, do not tolerate radiation very well. These are areas where cartilage lies close beneath the skin, as on the ears, or such areas as the fingers or the dorsum of the hand, where little subcutaneous tissue is present.

The following will illustrate some aspects of the treatment of patients with skin cancer at the M.D. Anderson Hospital. In patients with one or more small lesions, surgical excision with primary closure is usually performed because it is the fastest procedure. The patient can be ambulatory and surgery can be performed immediately after the diagnosis has been made. The surgical specimen is carefully checked to ascertain whether the borders and the base are free of tumor. If the pathologic examination shows inadequate excision, re-excision is carried out.

All lesions of the ear are excised. Small lesions of the helix can usually be removed by elliptical excisions followed by primary closure of the skin without resection of cartilage. Larger lesions of the helix or posterior aspect of the ear are removed by a v-shaped excision, and the remaining ear is shaped by additional triangular excisions from the region of the antihelix. Lesions of the concha can be excised easily even with the removal of the cartilage, and the defect can be covered by a full thickness skin graft. It is of utmost importance that the borders of the specimen adjacent to the ear canal be checked by frozen section. Subcutaneous extension of the lesion in this area is rather frequent (see figures 1 and 2).

Lesions that cover large areas of the skin of the face or of the scalp require wide excision and repair of the defect with a skin graft. Even resurfacing of the face is possible; indeed, it is frequently the only possible method of treatment. We see many patients with lesions of the skin of the nose who had been treated by electrocoagulation or radiation. It is extremely difficult to judge clinically the extent of the lesion in the scarred area. For this reason, and because we prefer to eliminate all changed skin, we very often completely remove the skin of the nose and repair

Fig. 5. *(Left)* Extensive basal cell carcinoma with loss of right lower eyelid and extension into the skin of the upper cheek. Patient had multiple treatments by radiation and electrocoagulation over many years. *(Center* and *Right)* After wide excision of tumor and repair of lower eyelid by tarsoconjuctival flap from upper eyelid and free graft of lid–skin to lower eyelid; full thickness skin graft to upper lateral cheek area.

the defect with a full thickness skin graft. Small lesions that require through and through excision and result in a defect of the tip or the ala of the nose can be repaired with a composite graft from the ear.

Large lesions of the nose which necessitate extensive resection are usually repaired after an interval of observation. Before reconstruction of the nose is performed, we wish to be fairly certain that no recurrence will appear locally. In general, the time intervals between excision and possible recurrence are very different and unpredictable. We feel that when the resection is sufficiently radical, a long period of observation, with its attendant hardship for the patient, is not justified. We prefer immediate repair, therefore, in those patients in whom we are reasonably sure that the resection has been sufficiently radical, and have reduced our period of observation. The best and fastest method for reconstruction of a large defect of the nose is by a forehead flap (see figures 3 and 4).

Lesions of the eyelids[5] are considered skin lesions because they usually start in the skin. Most patients with tumors of the eyelids can be cured either by surgical or radiation treatment. In small and medium-sized lesions, the functional and cosmetic results of both methods are about equally satisfactory. Thus, the choice of method in these cases will depend on other factors, such as the duration of disablement, hospitalization requirements, and the age of the patient. Our experience, though, indicates that for extensive tumors of the lower and upper eyelids, surgical treatment is preferable. The advantages of surgical treatment of patients with extensive lesions of the eyelids are manifold. The extent of these tumors cannot always be determined by clinical inspection; therefore, frozen section examination at the time of surgical intervention is of great value. Adjacent skin areas with multiple lesions can be excised widely and grafted at the same time. Irradiation always causes loss of the lashes and may cause teleangiecta-

Fig. 6. *(Left)* Extensive basal cell carcinoma of left lower eyelid, untreated previously. *(Center* and *Right)* After resection of lower eyelid and repair by tarsoconjunctival flap from upper eyelid and free skin graft.

sis, atrophic skin, and even ectropion. These changes become aggravated progressively while the good results after surgical treatment remain unchanged (see figures 5 and 6).

In conclusion, I should like to state the obvious: In skin cancer, as in cancer in general, the early, adequate, initial treatment determines the chances for cure.

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Old Instruments Wanted

The Medical Museum of the Armed Forces Institute of Pathology, celebrating its hundredth anniversary, is looking for items to complete its collection of instruments. Among those needed are microscopes dating from 1920 and instruments from the Confederate Army. The Institute cannot pay for these items but will preserve them in the collection, with proper credit given to the donor. Any person having instruments to contribute should write to the Director, Armed Forces Institute of Pathology, Washington 25, D.C.

Recent Advances in Pediatric Tuberculosis

Katharine H. K. Hsu, M.D., F.C.C.P.

THE ADVENT OF THE DRUG isoniazid (INH) has brought about a revolutionary change in the control of tuberculosis in children. Tuberculosis has become not only a curable disease but it has also become preventable. To the many children in the world who are sick and dying with this disease, and the many more who have been infected with tubercle bacilli, a new hope is born. The purpose of this paper is to disseminate the knowledge of this great advance in tuberculosis therapy so that many more children may be protected from the scourge of this dreadful disease. It has been estimated that it costs $10,000 to treat one child with tuberculous meningitis, but it takes only one dollar's worth of isoniazid to prevent it!

ISONIAZID—A POTENT ANTITUBERCULOSIS DRUG

The antituberculosis potency of INH has been thoroughly tested in the treatment of chronic pulmonary tuberculosis in adults. After 9 years of extensive clinical studies, INH has proved to be the most effective, and the least toxic, of antituberculosis drugs. For therapy of manifest forms of tuberculosis in children, INH has brought about results far superior to streptomycin.[1] Therefore, INH is now generally recognized as the primary drug for the treatment of tuberculosis. Streptomycin (SM) and para-aminosalicylate (PAS) are used as adjuvants.

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THE PREVENTION OF TUBERCULOSIS BY THE EARLY USE OF INH

Primary tuberculosis is the beginning of tuberculosis in the human body. The infection usually starts in the lung or the intestine, from where the tubercle bacilli are soon carried through the lymphatics and blood to become seeded in different tissues of the body. The primary infection and its seedings are potentially dangerous because they are the immediate precursors of all manifest forms of tuberculosis. In children, the most common manifestations are tuberculous meningitis, miliary tuberculosis, and progressive disease in the lung, the bone, and the intestine. The manifestations usually appear within a year or two following the primary infection.[2, 3]

During the past few years, a number of studies have been conducted in different parts of the world to determine whether the use of INH in children with primary tuberculosis will prevent the development of overt forms of the disease. The large-scale controlled study of the United States Public Health Service has clearly demonstrated that practically all the manifestations of tuberculosis in childhood can be prevented by the use of INH.[4] The extensive clinical observations made by "L'Institut National d'Hygiene" in France also proves the great preventive effect of INH.[5] At the Houston Children's Tuberculosis Hospital and Clinic in Texas, a study on the early use of INH in primary tuberculosis was started in 1953. Thus far, more than 800 children have been treated. After 7 years of continuous observation, we are quite convinced that the use of INH in primary tuberculosis will effectively prevent overt disease.[6, 7, 8]

INH is the first drug which makes possible successful chemotherapy of primary tuberculosis. Since hospitalization is not required for most children with primary tuberculosis, the only feasible therapy is the one which can be given at home both easily and safely. INH in tablet or liquid form meets these require-

ments. They are acceptable to the children because of the absence of any unpleasant odor or taste. Therefore, it can be expected that the drug will be taken with continued regularity. In our experience, toxicity is rarely seen in children. The only untoward reaction observed at our clinic was a skin rash due to an idiosyncrasy to INH; this occurred in four children.

Based upon the knowledge of the pathogenesis of tuberculosis in the human body and the antituberculosis effect of INH, it is now an established fact that prevention of tuberculosis is possible through the use of this drug. This means that a new approach has been opened in man's fight against tuberculosis.[9, 10] Prevention of the activation of tuberculosis in the millions of children who have already been infected by tubercle bacilli is a permanent necessity. It is now the responsibility of the doctors, nurses, and public health officers to find these children and protect them with INH therapy. The risk of developing active tuberculosis is particularly great among children who have been household contacts of a newly diagnosed contagious case. It is very likely that these children have become infected only recently. INH therapy for prevention of progressive disease is, therefore, especially urgent.

EARLY DETECTION OF PRIMARY TUBERCULOSIS BY TUBERCULIN TESTING

Tuberculin testing has assumed a new significance in this era of chemotherapy for tuberculosis. It is the only reliable test that reveals the presence of tuberculous infection before the roentgenographic evidence and clinical manifestations appear. Therefore, it has become a test of paramount importance for the early diagnosis of, and drug therapy for, tuberculosis in children.

Intradermal tests using purified protein derivative (PPD) in the amount of 0.0001 mg. is widely used the world over, although certain clinics prefer the use of the Old Tuberculin (OT). The test is read 48 to 72 hours later. Induration of 6 mm. or more is a positive test. Erythema without induration is a negative test. A large and intensive reaction indicates a greater likelihood of progressive disease than does a small reaction.

While the intradermal (Mantoux) test has been considered the standard technique for tuberculin testing, the difficulty of performing this test properly in children has greatly limited its use. A simple and painless device is urgently needed. The recently developed Heaf test by multiple-puncture technique has proved to be a satisfactory screening test.[11, 12] It does not frighten the children because there is no needle and syringe in sight. The technique is easy and simple. With one click of the "Heaf Gun" the test is over. In school surveys, we have been able to test 12 to 16 children per minute. The potency of Protoderm (PPD in glycerol—used in the Heaf test) corresponds very closely to 0.0001 mg. PPD. Reaction to the Heaf test, as a whole, is milder and more localized than to the Mantoux test. This technique will undoubtedly facilitate the wide application of tuberculin testing in children.

INDICATIONS FOR ANTITUBERCULOSIS THERAPY IN CHILDREN

Drug therapy is recommended in the following types of cases: (1) children up to the age of 3 years with a positive Mantoux test to 0.0001 mg. PPD; (2) children who have passed their third birthday and whose tuberculin reaction has converted from negative to positive within a year; (3) adolescent girls with strongly positive tuberculin reactions; (4) children with a positive culture of tubercle bacilli from the gastric contents, the urine, or a biopsy specimen; and (5) children showing roentgenographic or clinical manifestations of active tuberculosis.

Corticosteroids are known to reactivate old tuberculous lesions. All children who, for any reason, need a prolonged course of corticosteroid therapy should receive tuberculin tests first. If the reaction is positive, INH therapy should be given even though the tuberculosis is considered inactive. The duration of INH therapy should extend at least 3 months beyond the steroid therapy.

RECOMMENDED DRUG THERAPY FOR TUBERCULOSIS IN CHILDREN

Isoniazid (INH) is the most potent and the least toxic of antituberculosis drugs. It is essential to include INH in any treatment regimen of active tuberculosis. The duration of therapy should be at least one year. The administration of pyridoxine hydochloride for the prevention of neuritis does not appear to

be necessary in young children; however, it may be needed in adolescents.

For primary tuberculosis without roentgenographic or clinical manifestations, INH alone is considered a satisfactory treatment; PAS is not necessary. INH should be administered in dosages of 15 to 20 mg. per Kg. of body weight daily in two doses.

For localized manifest diseases in any part of the body, use INH combined with PAS. The dosage of INH should be 15 to 20 mg. per Kg. of body weight daily in two doses. The dosage of PAS should be 200 mg. per Kg. of body weight daily in two to three doses, not to exceed 12 Gm.

For miliary tuberculosis use triple drug therapy. Recommended dosages are as follows: SM—20 mg. per Kg. of body weight daily, with a maximum of 1.0 Gm. per day; INH—30 to 40 mg. per Kg. of body weight daily until miliary densities clear up on the radiograph, then reduce dosage to 20 mg. per Kg. of body weight thereafter; PAS—200 mg. per Kg. of body weight daily, with a maximum dose of 12 Gm. per day. SM is needed only in the acute stages of the disease. INH and PAS should be continued for at least one year from the time the miliary densities clear up in the chest radiograph.

For tuberculous meningitis use triple drug therapy. SM—20 mg. per Kg. of body weight daily, not to exceed 1.0 Gm. per day; INH—30 to 40 mg. per Kg. of body weight daily until spinal fluid becomes normal, then reduce the dosage to 20 mg. per Kg. of body weight (in children who vomit, parenteral administration of INH is advised to assure adequate intake); PAS—200 mg. per Kg. of body weight daily, not to exceed 12 Gm. per day. Streptomycin should be discontinued within one month after good clinical improvement; INH and PAS to be continued for at least one year from the time the spinal fluid returns to normal.

CORTICOSTEROIDS AS AN ADJUVANT TO ANTIMICROBIAL THERAPY[13, 14]

Administration of corticosteroids may hasten the resolution of the following types of disease conditions: pleurisy with massive effusion; obstructive emphysema or atelectasis due to large hilar nodes or endobronchial tuberculosis; miliary tuberculosis; and tuberculous meningitis. The dosage should be: Prednisone—1 mg. per Kg. of body weight daily for 4 to 6 weeks; for tuburculous meningitis, hydrocortisone is given intrathecally once a day for 2 to 4 weeks in a dose of 2.5 to 5.0 mg.

DISEASES CAUSED BY MYCOBACTERIA OTHER THAN TUBERCLE BACILLI

A number of acid-fast bacilli, which were previously considered saprophytes, have been recently discovered to cause tuberculosis-like disease in man. The most common manifestation seen in children has been lymphadenitis in the cervical and submaxillary regions. These lymph nodes have a great tendency to form abscesses. Acid-fast bacilli cultured from the pus differ from tubercle bacilli in that they are nonpathogenic to the guinea pig. Because of this difference, these acid-fast bacilli are currently known as "atypical Mycobacteria." Increasing varieties are being isolated from sputum, pus, and the surgical specimens from adult patients. Currently they are classified according to the pigment development of the culture and the rate of growth. Response to drug therapy varies greatly with the species of organism involved.

SUMMARY

1. Tuberculosis in children can be prevented by INH therapy of primary tuberculosis. It is to be deplored now more than ever before that children develop this dreadful disease.

2. Tuberculin testing has assumed new significance because it is the only reliable diagnostic test for detecting tuberculosis before it becomes manifest.

3. Household contacts of a recently diagnosed contagious case should be given priority for preventive INH therapy if the treatment facilities in the community are limited.

4. The use of INH has greatly improved the result of treatment of manifested forms of tuberculosis in children.

5. Indications for drug therapy and the therapeutic regimen recommended for children are given.

6. Mycobacteria other than tubercle bacilli may produce tuberculosis-like disease in children. Some of these Mycobacteria are resistant to antituberculosis drugs currently in use.

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Physician Blames Parents of Alcoholic Individuals

A Salem, Va., physician who has talked to more than 13,000 alcoholics says that most of them apparently missed "the adventure of self-reliance." Writing in the September, 1959, issue of *GP* magazine, Dr. Albert J. Russo, Medical Director of Salem's White Cross Hospital for Alcoholics, puts much of the blame on parents who did not let children "accept the challenges of day-to-day living."

"Somewhere along the line from childhood, in rich and in poor families, an overindulgent parent deprived a nice little boy or girl of the adventure of self-reliance. All their activities were regulated into don't-do-this or don't-do-that," Dr. Russo contended.

As for the treatment of alcoholic individuals, Dr. Russo stated that sedatives should always be controlled by someone other than the patient. Offered either medicine or whisky, the alcoholic will consume large amounts. Some alcoholics have died because they mixed capsules and whisky or took a hypodermic from a physician after denying that they had earlier consumed alcohol or sleeping pills.

Some Diagnostic and Therapeutic Problems of the Superficial Mycoses

Rachel Ford Spiller, M.D., and William Fielding Spiller, M.D.

ALTHOUGH FUNGI WERE among the earliest recognized microscopic agents causing disease, tineal infections and their differential diagnosis are still among the conditions most puzzling to the nondermatologist. We will describe some points infrequently stressed in the diagnosis and treatment of fungous infections. Lack of knowledge of these points frequently contributes to an erroneous diagnosis or lack of cure. We hope that emphasizing these characteristics, which are so familiar to the dermatologist, may be of help to the nonspecialist.

With the development of systemic antifungal therapy (griseofulvin), the correct diagnosis of fungal diseases is even more important if medical practice is to maintain high standards and avoid unnecessary expense to the patient. Neither griseofulvin nor topical antifungal preparations should be used before making an accurate diagnosis because they may interfere with laboratory tests (suspension in KOH solution and culture), and be ineffective therapeutically or even harmful. Examination of skin scrapings prepared by clearing in 10 to 20 per cent potassium hydroxide in aqueous solution and cultures on Sabouraud's glucose agar should be taken at the initial examination of the patient to determine the causative agent.[1, 2] This can easily be done in any office with proper materials and training. There are too many diseases in which the pathogenesis is unknown and the diagnosis more difficult for the physician to be lax in those areas where accuracy is possible by identification of the etiologic agent.

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It is important to realize that all round or oval lesions are not "ringworm," and that there are numerous conditions that can produce similar morphological pictures. The diseases most frequently referred to us with a mistaken diagnosis of ringworm are: pityriasis rosea (herald patch and the widespread eruption), seborrheic dermatitis, xerosis, nummular eczema, contact dermatitis, dyshidrosis and vesicular eruptions of the hands and feet, impetigo and secondary bacterial infections of the feet, achromia parasitica, and granuloma annulare. The importance of finding fungi in the KOH suspension and confirming a clinical diagnosis of ringworm cannot be stressed too much. Likewise, negative results (and repeated scrapings may be necessary) are equally important to rule out a tineal infection in many of the above enumerated conditions since they may clinically appear similar. Annular configuration of the lesions may occur in any of these. The epidermal reaction of scaling, which occurs in pityriasis rosea, seborrheic dermatitis, xerosis, and nummular eczema, as well as the vesiculation and scaling in contact dermatitis, dyshidrosis, and impetigo may not be differentiated by clinical appearance alone, and examination of the KOH suspension may be necessary for a correct diagnosis. The absence of any epidermal reaction in granuloma annulare, unless the lesion has been irritated by topical medicaments, makes the differential diagnosis easy for the experienced observer. However, with complicating factors and in atypical cases, a negative finding in KOH suspension and culture as well as a biopsy may be necessary for an accurate diagnosis of this condition.

Xerosis, the scaling lesions of the skin due to excessive dryness, may be aggravated by

the topical application of medicaments that produce peeling and exfoliation, which might be used in the treatment of tinea. Also, washing with soap and water may aggravate xerosis, nummular eczema, and pityriasis rosea whereas it would be indicated in cases of tinea or bacterial infections, indicating further the importance of a correct diagnosis before treatment is instituted.

Inverse lesions of pityriasis rosea, atypical localization and distribution, and the herald patch prior to the onset of the general rash are often difficult to differentiate from tinea, and in such cases a negative finding in the KOH suspension and culture are frequently of real value. Conversely, extensive eruptions of tinea corporis resembling pityriasis rosea have been diagnosed by finding mycelia in the KOH suspension. Suspicion should be aroused in the unusual case.

Differentiating the lesions of seborrheic dermatitis from those of tinea corporis may present a problem even for the experienced dermatologist. Without laboratory assistance scaly lesions on the scalp may be indistinguishable from those caused by *Trichophyton tonsurans* and the lack of the brilliant green fluorescence, characteristic of infections by *Microsporum canis* and *M. audouini*, makes a search for broken off or "black dot" hairs necessary. Isolated annular and patchy lesions of seborrheic dermatitis on the glabrous skin may also present a problem.

The location, history, and duration of lesions of nummular eczema may help one in being suspicious of the diagnosis. A negative KOH suspension test will help to avoid the use of irritating fungicides and the needless expenditure of money for medicaments.

Patients have frequently been referred to our office with the diagnosis of tinea pedis when the problem is one of contact dermatitis to shoes. The location on the dorsum of the toes is an especially valuable clue since tinea pedis rarely involves only the upper surface of the toes, leaving the intertriginous areas clear. Contact dermatitis of other areas of the body due to metal sensitivity may also simulate tinea corporis with annular lesions.

Dyshidrosis (or pompholyx) is another thought-provoking eruption that is frequently mistakenly called a fungous infection. Observation of the course of the process and again negative laboratory examinations are necessary to rule out a fungous infection or "id" reactions to a fungus. Clinically, it would be very unusual to have the deep-seated, sago-grain vesicles on the palms and soles without also having the superficial scaling and intertriginous maceration and scaling characteristic of tineas. Acute vesicular reactions of the feet frequently become secondarily infected by bacteria and treatment for the bacterial infection must be instituted to alleviate this element of the problem. The acute reactions should have local therapy consisting of compresses, rest, and elevation of the feet. Irritating antifungal preparations are best avoided.

The infection of the fine hair covering the body (lanugo hairs) in patients with tinea corporis may be responsible for recurrences and necessitate prolongation of treatment. Although examination of the body under Wood's light in cases of tinea corporis is generally not helpful, it is well worth the effort when the characteristic fluorescence of lanugo hairs is found. This establishes the diagnosis and indicates that therapy must include treatment of this skin appendage. Early detection and manual epilation of involved lanugo hairs may speed the process of recovery. If griseofulvin is given, it must be continued long enough for the eradication of this source of infection.

Reinfection from involved nails has been stressed by numerous authors and by the manufacturers of griseofulvin in listing recommended dosage. Robinson and co-workers[3] have stated that cultures from the distal end of the nail may remain positive even when the growth of the new nail is almost complete (about 11 or 12 weeks for fingernails and longer for toenails). We have seen the rapid development of fingerlike infected processes extending into the normal appearing nail from the diseased distal portions. We feel that debridement of the hypertrophic, crumbly, and discolored nail is to be recommended. This will help to reduce the amount of infective material, which may be important since griseofulvin is fungistatic instead of fungicidal.

Although griseofulvin has been an invaluable discovery, the usual routine care of tinea capitis should also be recommended. Shaving the scalp, daily shampoos (diminishing to every other day) and careful covering of the scalp with a clean boilable cap each day, should be employed for epidemiologic reasons, prevention of recurrences, and possibly to shorten the course of treatment. The use

of topical fungicides, such as undecylenic acid; salicylic acid; and copper, sulphur, or iodine compounds may also reduce the contagion from the surface material in tinea capitis and corporis and may speed recovery. Alternating the topical fungicides has been recommended to help prevent the development of resistance to the medication by the organism.[4] Tinea capitis due to *Microsporum canis* (*lanosum*) treated with griseofulvin may occasionally show a slow response. The usual topical treatment in the cases due to this organism may be especially important. We agree with Wilson[4] in his theory of the value of topical therapy: Although topical fungicides do not penetrate the follicle, they may reduce "the amount and the vigor of the 'parent' mycelial stock at the surface of the follicle, thereby causing a slowing of the rate at which the terminal penetrating hyphal filaments grown downward." It is of benefit to combat this disease from every possible direction.

It is also important to realize that kerion, the marked inflammatory reaction to the fungi, can develop in patients already on griseofulvin therapy. It has been established that an inflammatory reaction is a good sign that the patient will get well[5] in spite of its appearance to the parents. It remains to be statistically proved whether griseofulvin therapy will shorten the duration of the inflammatory reaction in tinea capitis since this varies with the infecting organism and the individual's response. Hot packs are indicated for the marked inflammatory and boggy reactions.

In *Microsporum* infections fluorescence may be obscured or changed by treatment. The absence of fluorescence does not mean cure, and patients should not be considered well until after cultures or microscopic examinations have been found negative. New hair growth usually becomes apparent in three weeks after initiation of griseofulvin therapy; and by five weeks the infection is cleared, in most cases, if the old infected hairs have been cut off. It has been possible to obtain positive cultures and KOH suspensions from the free ends of hair in the infected areas until the hair has been replaced by healthy new growth. On KOH examination, the hyphae in the hair shaft show curling and shriveling. Since griseofulvin seems to be fungistatic, not fungicidal, a source of reseeding is available unless infective material is removed.

Of the superficial fungous infections, tinea versicolor and monilia do not respond to the administration of griseofulvin systemically. Lesions of tinea versicolor found in unusual locations, such as on the face, at the edge of the scalp, and in isolated patches may require a positive laboratory examination. The typical short hyphae and grapelike clusters of organisms make a diagnosis possible, although in the usual case of tinea versicolor, the clinical characteristics of the disease are so distinctive as to be pathognomonic without laboratory studies. Frequently, a monilial infection is suggested by the KOH examination and the clinical picture; however, a culture may be necessary for diagnosis. Griseofulvin therapy has been reported to aggravate monilial infections.[6]

SUMMARY

In the recent literature there have been numerous articles about the new oral antifungal medicament, griseofulvin, but relatively few have dealt with the diagnosis of tineal infections. Some points infrequently stressed concerning the differential diagnosis of the skin lesions and therapeutic suggestions for treating superficial fungous infections have been presented. The importance of positive laboratory confirmation of tineal infections has been emphasized.

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Respiratory Distress in the Newborn Patient

Murdina M. Desmond, M.D.

SINCE MORBIDITY OR DISEASE in the neonatal period is uniquely difficult to assess, the extent or limits of disease in the neonate can only be estimated at the present time. For this reason in part, the evaluation of the effects of maternal diseases, complications of delivery, and obstetrical procedures are based on perinatal mortality, rather than on both perinatal mortality and neonatal morbidity. It is customary also to classify difficulties in the infant on the basis of maternal history such as "infants of diabetic mothers," or on events of delivery such as "infants delivered by Ceasarean section," rather than on the basis of physical findings in the infant.

Finding the origin of neonatal disease is a complicated undertaking. First, neonatal disease developing soon after birth occurs during a period of momentous change in the organism. The baby, upon delivery, begins to undergo a series of major physiologic changes necessary for extrauterine existence. Accompanying these physiologic changes are a group of physiologic findings which in other age groups might connote the presence of a disease process: fall in body temperature,[1] fall in blood pressure,[2] high polymorphonuclear count,[3] presence of transient murmurs,[4] fall in blood glucose,[5, 6] and acidosis (metabolic and respiratory).[7]

Second, the infant at delivery has been involved for some hours in the process of labor, a process with many variables for the infant. There is evidence to suggest that even normal birth may be accompanied by a brief period of asphyxia.[7,8,9] In addition to the effects of the birth process must be added the possible effects of pharmacologic agents (anesthetics, analgesics, diuretics, etc.) and obstetrical procedures utilized during labor and delivery. If anesthetics and analgesics have been employed, and have been transmitted to the infant, then the infant must recover from the effects of these after delivery.

Therefore, if a disease process is present in the neonate it must be viewed as an additional problem occurring during a period of transition (intrauterine to extrauterine life) and during a period of recovery (asphyxia, drug effects, etc.). The equivalent patient in adult medicine would be the postoperative patient.

Disease processes in the neonate appear to be of two basic types. The disease process may be within the infant from birth, or may have existed within the intrauterine environment prior to delivery. In other terms, the disease process may be intrinsic or within the infant, or extrinsic, outside of the infant. In the former the disease process may affect the infant prior to delivery but more often begins only when the infant is called upon to function after delivery. In extrinsic disease the infant is separated from the abnormal intrauterine influences with the act of delivery and his problem is therefore one of recovery. The classification of neonatal disease given in the following tabulation is based largely upon the work of Gruenwald[10] and Morison.[11]

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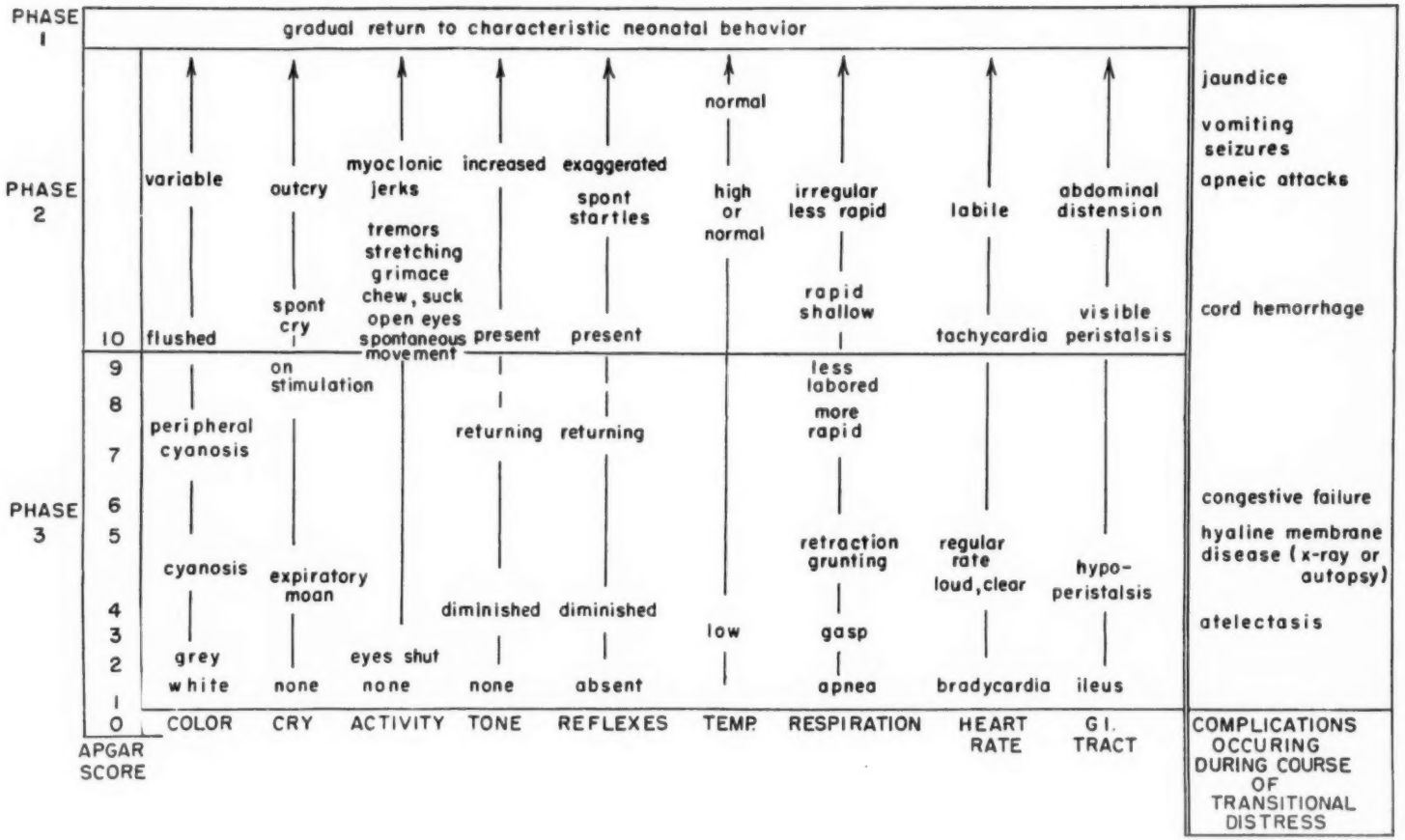
A CLASSIFICATION OF NEONATAL MORBIDITY

1. *Intrinsic Disorders:* within the infant and continuing from birth—congenital anomalies, infections, anemias, incompatibilities between mother and infant, birth injuries, and genetic disorders.

2. *Extrinsic Disorders:* source in an abnormal intrauterine environment, with infant separated from source with delivery—position of

TABLE I
Transitional Distress of the Neonate



comfort anomalies, drug effects, drug withdrawal effects, effects of maternal pathophysiology, effects of anoxia and asphyxia, and intrauterine growth disturbances.

3. *Combined Intrinsic and Extrinsic Disorders*

4. *Unknown*

The disorders discussed in this report are those which manifest respiratory symptomatology. This is the most common type of difficulty seen in a nursery. Many disorders involving systems other than the respiratory system are first brought to the attention of the physician because of their association with disturbed respiration. Respiratory disorders may be classified as intrinsic or extrinsic in accordance with the classification given above. Although intrinsic disorders are less common than extrinsic disorders, it is most important to diagnose intrinsic disease early since these disorders comprise most of the neonatal "emergencies" for which we have specific therapies at the present time.

EXTRINSIC DISEASE

During the course of observation of newborn infants it has been noted that a group of signs of difficulty occurred in a definite sequence, and that the sequence had both cardiopulmonary and neurologic components. Infants who were improving clinically followed the sequence of symptomatology in one direction, while infants who were deteriorating clinically, followed the sequence of symptomatology in the reverse direction. These signs and symptoms were readily divisible into phases. Since the symptomatology resembled the well-documented symptomatology shown by patients recovering from anesthetic, anoxic, and hypoglycemic depressions, it was assumed that these symptoms represented also the recovery from a prior cerebral depression. The phases were graded numerically in the manner customarily used for the grading of the stages of anesthesia, anoxia, etc. The total symptomatology, with cardiopulmonary and neurologic components in all three phases, is shown in table I. The combined sequences have been previously reported as Transitional Distress.[12,13] It was postulated that in the infant in whom the difficulty occurred immediately after birth, these clinical changes reflected the recovery of the neonate from the depression suffered during or prior to delivery, as a result of asphyxia and of drugs (anesthesia and analgesia) administered to the mother.

In the recovery sequence, (phase 3-2-1) respiration proceeds from apnea, to gasping, to grunting, and finally to a rapid regular type of respiration. Heart rate progresses from a bradycardia, to a fixed regular rate with loud clear sounds, to a tachycardia, which initiates the onset of phase 2.

During the course of phase 3, the infant shows a gradual recovery from a hypotonic, hyporeflexic, unresponsive state. At the onset of phase 2, tonus and reflexes are present. In the upper portions of phase 2 evidences of neural excitation with hypertonicity, hyperreflexia, and spontaneous hyperactivity are seen.

Temperature tends to be low during phase 3 with an increase to normal or above normal during phase 2. Bowel function changes from hypoactivity (ileus) in lower phase 3, to hyperperistalsis and thence to abdominal distension associated with tight anal sphincters in phase 2.

During the course of recovery, certain complications tend to occur (Table I). These complications may create a new problem for the infant, and may become decisive in the outcome. It is interesting that the complications appear to reflect changes in specific organ systems. This is in agreement with the statement of James[7] that asphyxia is a generalized disease affecting all body tissues.

Infants with low Apgar ratings[14] at one minute after delivery manifest this sequence of symptoms. As the infant improves, the Apgar rating tends to increase; if the condition of the infant deteriorates, the Apgar rating tends to become lower (see Comparison of Apgar Score with Recovery Sequence as shown in table I).

The clinical course of the infants may follow a variety of pathways. Some appear to be in excellent condition at birth, but grunting and retractions appear (phases 2-3) within a short time. The infant may then improve (phases 3-2-1) or may remain in phase 3 until death. Other infants progress successfully through phase 2, only to develop a prolonged seizure with apnea in upper phase 2. With apnea and cyanosis the infant reverts quickly to phase 3.

Hyaline membrane disease (the presence of hyaline membranes in the lungs of infants dying during the immediate neonatal period) cannot be classified as either extrinsic or in-

trinsic in origin at the present time. Both intrinsic and extrinsic factors have been implicated.[7, 12, 27] The disease found at autopsy and its clinical correlates may represent a combination of intrinsic and extrinsic factors, which operate most frequently in conjunction with premature birth, maternal diabetes, and birth asphyxia.

INTRINSIC DISEASE

Infants with intrinsic disease may also show evidences of some or all of these manifestations described above, if the intrinsic disease interferes with oxygenation and hypoxia, or if asphyxia becomes part of the clinical picture. When this occurs the differential diagnosis of intrinsic disease and extrinsic disease becomes more difficult. Reliance must then be placed on the history, on specific findings in the clinical examination which are typical of the disorder in question, and on the roentgenographic findings.[15]

The physical examination of a distressed infant is frequently difficult to perform since the infant often appears to react adversely to handling, particularly if examined outside the incubator. A system of examination, which may be done rapidly within an incubator while the infant is in an oxygen-rich atmosphere, is presented herein. The first portion of this examination is visual; the second portion may be readily carried out through the portholes of the incubator. The maneuvers of this examination will permit the examiner to detect most of the specific findings of the most frequently encountered intrinsic diseases.

Findings suggestive or specific of intrinsic disease producing respiratory difficulties in the immediate neonatal period are listed in table II. These are findings which are not common to the uncomplicated recovery process associated with birth depression.

TABLE II
Intrinsic Disease with Respiratory Symptomatology

Disorder	Characteristic Findings on Physical Examination	Tends to Occur in Association With	Reference
Nasal Obstruction	Dyspnea and subcostal retraction in supine position Inspiratory click as tongue seals the airway briefly Retraction of head Diminished air flow through nostrils Mechanical inability to suck for usual periods	Choanal Atresia Reserpine administration to mother, nasopharyngeal masses	16 17 18
Laryngeal or Upper Tracheal Obstruction	Stridor or aphonia Violent deep retraction of subcostal and supraclavicular areas Poor aeration bilaterally	Laryngeal or tracheal stenosis or atresia Tumor masses Vascular rings	18
Pneumothorax	Asymmetry of chest Poor aeration, restricted chest movement on involved side Depression diaphragm on involved side Shift of apical impulse to opposite side	Difficulty in establishing respiration at birth Endotracheal resuscitation	19 20
Pneumomediastinum	Distant heart tones, with good peripheral pulses Distension of neck veins Apical impulse not readily palpable	Pneumothorax Subcutaneous emphysema Interstitial emphysema	21 20
Meconium Pneumonitis	Meconium staining of amniotic fluid, skin, and nails of infant Coarse irregular opacties on chest roentgenogram Increased A-P diameter of chest	Meconium stained amniotic fluid Term delivery	22 15
Interstitial Pulmonary Emphysema (Air Block)	Chest fixed in inspiratory position Increased A-P diameter Depression of diaphragm	Poor condition at birth Resuscitative measures	21

STEPS IN THE EXAMINATION OF THE DISTRESSED NEONATE

Outside Incubator: Note contour, symmetry, and movement of thoracic cage

Note color, central and peripheral; note uniformity of color in body areas

Count respiration for a full minute, noting character and rhythm of respiration

Inside Incubator: Place stethoscope over nose and mouth, noting passage of air, duration of inspiration and expiration, and abnormal respiratory sounds

Localize maximal apical cardiac impulse with whole hand

Count apex rate of the heart for one minute—note regularity, quality, and intensity of sounds

Stethoscope to chest for extent of air exchange

Measure liver size in midclavicular line

Palpate femoral and brachial pulses

Check tone and reflex responses—

(1) tone: gently extend lower extremities

(2) reflex responses (a) toe grasp, (b) stroke upper lip lightly, noting movement of lips and tongue

SUMMARY

The complexities surrounding the diagnosis of respiratory problems during the neonatal period are discussed. Diseases of the neonate which give rise to respiratory symptomatology are divided into four groups, that is, intrinsic, extrinsic, combined intrinsic and extrinsic disorders, and disorders of unknown etiology. Intrinsic disorders, although less frequent, comprise most of the treatable emergencies of the neonatal period.

Extrinsic disorders, originating in an abnormal intrauterine environment, are more frequently encountered. The source of difficulty is removed at delivery with the separation of the infant from his unfavorable environment. The process of recovery undergone by the infant is reflected in a sequence of cardiopulmonary and neurologic symptoms. The total symptomatology, divided into three phases, is termed "Transitional Distress." Similar se-

TABLE II
(Continued)

Disorder	Characteristic Findings on Physical Examination	Tends to Occur in Association With	Reference
Cardiac Failure	Cardiomegaly Hepatomegaly Poor quality of heart tones Periorbital edema	Congenital heart disease Large left to right shunts Congenital pneumonia Intrauterine anemia	23
Congenital Pneumonia	Excessive mucus, tachycardia, tachypnea, hyperthermia or hypothermia Infant limp, jaundiced, and lethargic	Febrile mother, prolonged rupture of BOW Fetal tachycardia	24 20
Diaphragmatic Hernia	Shift of apical impulse Diminished movement of chest and aeration of chest on involved side Scaphoid abdomen		20
Tracheoesophageal Fistula	Constant excessive mucus Choking and cyanosis on feeding Immediate regurgitation of feeding		18
Unilateral Paralysis of Diaphragm	Progressive dyspnea, see-saw movement on inspiration Elevation diaphragm on involved side Absence abdominal movement on inspiration	Brachial palsy	25
Massive Atelectasis	Bell-shaped thorax, obstructive respiration	Fetal anoxia	15
Anemia Due to Blood Loss	Pallor, tachycardia, and rapid shallow respiration Above followed by shock	History of abruptio placenta, placenta praevia, incision into placenta. Abrupt onset of symptoms with bleeding into viscus or into tissues when onset occurs later in neonatal period	26

quences are shown by infants with intrinsic disease, if the intrinsic disease tends to bring about hypoxia or hypercapnia in the infant.

The differential diagnosis of intrinsic and extrinsic disorders are discussed, and the more frequent physical and roentgenographic findings of intrinsic diseases are listed.

An outline for the rapid physical examination of a distressed infant is presented.

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President's Message

Like any human being, I feel a need for concrete evidence that "Ryder has been here." In my mind, there are two ways that this can be done. One is through memorials, buildings, or other tangible evidence of what has been achieved. The other is the intangible, the ephemeral, like the "good will" that can accompany an organization. The latter is, for an organization, good sound administration, steady growth, and, most important of all, the working together for common goals. It is the latter I want for the AMWA as my evidence.

As an example of what I mean, in public health, we today face the serious problem of the chronically ill and older individual. All too often in a community it is not a matter of a lack of facilities and resources, it is the lack of co-ordinating these facilities that allows people to fall in the "cracks." A person is isolated and filed away in a nursing home because there are no community services for home care, or ends up in a general hospital bed that should be occupied by an acutely ill person, because there is no homemaker service to allow that person to go home. Or these services may be available, but only to a small group of persons. So, in public health, we have been talking to communities about the goal of developing a "co-ordinated community care" program. The goal here is continuity of care, comprehensive and adequate both as to quality and quantity.

When we approach a community now that has many services and programs for the chronically ill, and yet still has a problem, we suggest that it take four steps. First, that it settle down and determine what it has in the form of resources; secondly, that it determine the needs of the people in the community; thirdly, that it attempt to match up these two items (this will indicate the gaps, and, more important, the overlappings); and finally, that it set up a plan of action that includes a built-in priority schedule.

You know, in public health, we used to go out to sell certain glamorous programs: multiple screening, for example. We approached small communities with these tremendous plans. "Isn't it wonderful that you can have a long screening line, and you can have 22 tests, and people can go through there and in an hour and a half you will know all about them?" The small community looked at it and said, "But we don't have any nurses," and "We don't have an outpatient department," and so on. Well, we grew up. We came to realize that you must tailor the program to the community. You do not put out a smörgasbord and say "Come on boys—take your choice." If you have ever had smörgasbord you know what can happen: you take your plate, you fill it up and then when your plate is full, you see the thing you really want.

(Continued on following page)

The plan is the most important step in community organization. Setting a plan in motion cannot be done by a single person. It cannot be done by a group of individuals working independently. It results from a complete understanding of the situation. Yesterday I started the discussion by saying, "If you aren't thoroughly confused, you don't understand the situation." I think we need this growing up together, perhaps getting confused and then working through the problem, so that there is an acceptance, because you know we don't move into action just by hearing something. We move into action only if we are motivated to do so.

I have thought of many terms that we could use. The National Health Council came out with one that will do very nicely. Their annual report of two years ago came out with a very startling cover—"2 plus 2 equals six, 3 plus 3 equals nine, x plus y equals infinity." And the title was Synergism.

I looked up the definition of this word, and found that it usually refers to muscular action. A single muscle contracting gives you so much motion, a second muscle contracting gives you additional motion, and if you contract the two together the sum of action is more than would have been achieved with individual action. This is what I would like our association to think about this coming year. I would like to see us working together synergistically. I would not be in the public health field if I had to have buildings and memorials left to attest to the fact that I have made an impact. I am in Public Health so that 20 years after I have been to a community someone can say, "Do you remember the day you were here and said something about rehabilitation to us? We just opened up our first center." That is satisfying enough to me. Next year I would like to see us concentrate on evaluating our resources and our needs, determining our gaps and overlappings, setting up a plan with priorities, and then when Dr. Brown gets into office, she can take the plans and go into action. *(From remarks made at the AMWA Interim Meeting, Washington, D.C., Dec. 4, 1960)*

Claire F. Ryder M.D. M.P.H.

GOLDIE SUTTLE HAM, M.D.

The Houston Branch of the American Medical Women's Association is honored to pay tribute to this outstanding member whose wonderful philosophy is, "You should earn your way with something you feel joy in doing."

Dr. Ham was born in Georgia but moved to Greenville, Miss., at an early age. She received her grade and high school education there and then went to Agnes Scott College in Atlanta, Ga., where she graduated with a B.A. degree. While in college Dr. Ham also studied music and participated in athletics and various other activities. She served as president of the Athletic Association and the YWCA and was a member of the Mortar Board.

After her graduation from Agnes Scott College she entered the medical school of Tulane University in New Orleans and received her medical degree in 1923. She then served an internship at Charity Hospital in New Orleans. While interning she met Dr. P. H. Scardino of Houston, Texas, who was there learning about the new Insulin therapy. He had a large practice in Houston and convinced her that Houston was a good place in which to begin the practice of medicine.

After serving her internship she proceeded to Houston and a residency at St. Joseph's Hospital, being the first woman resident in Houston. (St. Joseph's Hospital at that time was the largest hospital in Houston; it is still one of the larger hospitals and is the third largest maternity hospital in this country.) Here she became acquainted with the physicians in Houston and was graciously accepted by them.

It was remarked that she never appeared conspicuous, never exhibited her professional knowledge for the mere purpose of show, although she was always resourceful when occasion required it. She went about her work with a quiet dignity that inspired confidence.

After her residency at St. Joseph's Hospital Dr. Ham became associated with Dr. Scardino, whose practice was large, and as a consequence she obtained the rich and varied experience to develop her skill in surgery. In 1930, however, she limited her practice to obstetrics and gynecology.

She has continuously been active on the obstetrical staffs of Jefferson Davis (City-County Hospital) and St. Joseph's Hospital, and is now on the consulting staff of both hospitals. She was active for many years with the Health Department of the city; at one time a member of the Board of Health. Dr. Ham has also actively supported the civic life of Houston—Planned Parenthood, League of Women Voters, YWCA (at one time a member of the Board), Houston Symphony Society, Museum of Fine Arts, and the Houston Opera Association.

In 1932 Dr. Ham married Gordon Bell Hanson, who is president of the Howe-Baker Corporation. She took time off from her evergrowing practice to rear two daughters, both of whom are now married. She has two granddaughters.

In January, 1960, she gave up her obstetrical practice, took a Caribbean cruise, and returned to the practice of gynecology.

Dr. Ham and her husband own a small country estate on the edge of Houston, where she actively engages in her various hobbies such as gardening, sewing, horseback riding, and fishing.

It is with pleasure that the members of this branch of the AMWA spotlight Dr. Goldie Suttle Ham. —*Benjy F. Brooks, M.D.*

Opportunities for Women in Medicine

COURSES

Alcohol Studies. The 1960 session of the Yale Summer School of Alcohol Studies will be held June 25-July 20, 1961, in New Haven, Conn. Lectures, workshops, and seminars will comprise the interdisciplinary study of problems of alcohol and alcoholism in society. For information, the Registrar of the Summer School may be contacted at 52 Hillhouse Ave., Yale Station, New Haven, Conn.

Medical Care and Public Health in Norway. The University of Oslo, Norway, 1961 summer school session will include a special course on problems of medical care and public health in Norway. The session goes from July 1 to August 11. Catalog and application forms may be obtained from the Oslo Summer School Admissions Office, c/o St. Olaf College, Northfield, Minn. The final date for consideration of applications is March 15, 1961.

Surgery of the Hand. New York University Medical Center is presenting a five day, full-time course on surgery of the hand, March 6-11, 1961. All facets of modern hand surgery, including anatomy, physiology, diagnosis, surgical techniques, and management of hand lesions will be covered by the NYU and guest faculties. Applications may be obtained from the Associate Dean, NYU Post-Graduate Medical School, 550 First Ave., New York City 16.

FELLOWSHIPS

Obstetrics and Gynecology. The American Association of Obstetricians and Gynecologists announces the establishment of the James W. Kennedy Memorial Travel fellowship, providing $6,000 for a year of graduate study in a foreign country in obstetrics and gynecology or an allied field. Candidates must have had a minimum of three years of residency training in obstetrics and gynecology, and may be full-time members of a department of obstetrics and gynecology of a medical school in the United States or Canada. Applications may be obtained from Dr. Francis B. Carter, Chairman of the Committee, Dept. of Obstetrics and Gynecology, Duke University Medical Center, Box 3705, Duke Station, Durham, N.C. The deadline for completed applications is March 1, 1961.

Steroid Biochemistry. Specialized programs have been established in Worcester, Mass., and Salt Lake City, Utah, to train investigators on both the post- and predoctoral levels in the theoretical and methodological aspects of the biochemistry of steroids and related compounds. Lectures, planned laboratory work, and research will be offered. The Worcester Foundation for Experimental Biology, Shrewsbury, Mass., with Clark University, Worcester, and the University of Utah, Salt Lake City, is presenting the training programs under the sponsorship of the National Cancer Institute, National Institutes of Health, U.S. Public Health Service.

Postdoctoral fellows will receive stipends of $5,500 for a one-year period; predoctoral fellows (accepted only at Worcester) will receive stipends of $1,800 for a six-month period. The final date for receipt of completed applications is June 1, 1961. Information and applications may be obtained from either of the following: Dr. Kristen Eik-Nes, Department of Biochemistry, College of Medicine, University of Utah, Salt Lake City, Utah; Dr. William R. Nes, Department of Chemistry, Clark University, 950 Main St., Worcester, Mass.

MEETINGS

Allergy. The seventeenth annual congress and postgraduate course of the American College of Allergists will be held in Dallas, Texas, March 12-17, 1961. Information may be obtained from Dr. John D. Gillaspie, Treasurer, 2141 14th St., Boulder, Colo.

Psychoanalysis. "Distorted Communication in the Psychoneurotic" will be the subject of a panel discussion at the New York Academy of Medicine, New York City, on Feb. 15, 1961, at 8:30 p.m. The speakers include Drs. D. A. Barbara, Martin Symonds, R. L. Sharoff, and J. A. Meerloo. The program is presented by the Association for the Advancement of Psychoanalysis.

News of Women in Medicine

Dr. Frances A. Allen of Newton, Kan., is serving as president of the Greenwood, Kan., Medical Society for 1960-1961.

Among the faculty of the thirteenth annual postgraduate course on diseases of the chest—"Recent Advances in the Treatment of Diseases of the Heart and Lungs"—sponsored by the American College of Chest Physicians and held in New York City, were the following women physicians: Drs. Dorothy H. Andersen and Julia Jones of Columbia University College of Physicians and Surgeons; and Dr. Edith Lincoln, of New York University College of Medicine. All are from New York City.

"Japanese Vegetables," an essay, won for Dr. Elizabeth B. Anderson, of the Oak Ridge Institute of Nuclear Studies, the rank of runner-up in the 1960 annual contest in nonmedical writing sponsored by the American Medical Writers' Association. Certificates were presented to the winners at the Association's annual meeting in November, 1960.

Dr. Beatrice B. Berle of Bellevue Hospital, New York City, a participant at the 1960 White House Conference on Children and Youth, discussed the effects of the population's mobility on the health of young persons.

Dr. Bertha A. Bouroncole, Associate Professor of Medicine at Ohio State University, was on the faculty of the American College of Physicians' postgraduate course, "The Place of Hematology in Internal Medicine: With an Introduction to Radioisotope Technics and Their Application." The course was presented in September, 1960.

Dr. Madelaine Ray Brown of the Harvard Medical School was featured in the Oct. 26, 1960, issue of *Scope Weekly*. Dr. Brown, who has had multiple sclerosis for almost 33 years, was shown conducting a seminar, attending a lecture, and reading with the help of a push-button page turner.

Dr. Jale Duvenci, formerly Research Associate and Charlton Fellow at the Tufts Lung Station of Boston City Hospital, has returned to Ankara, Turkey, where she will teach and do research in diseases of the chest.

Dr. Alice Ettinger, Roentgenologist-in-Chief at the Pratt Clinic-New England Center Hospital and Professor and Chairman of the Radiology Department at Tufts University School of Medicine, was featured in a recent issue of *Scope Weekly*. She first came to the United States in 1932 as a Bingham Fellow. " 'Years and years later,' she says with a smile, 'I learned that when Dr. Pratt heard who was coming over, he asked, "Haven't you got a man?" ' "

Dr. Lydia G. Giberson, Assistant Vice-President of Metropolitan Life Insurance Co., was voted "Outstanding Professional Woman of the Year" for 1960 by the Business and Professional Women's Clubs of New York State.

Drs. Ruth J. Guttmann and R. Dorothy Sundberg were among the speakers at the 1960 annual session of the Medical Society of Michigan.

Dr. Elizabeth Mason Hohl of Los Angeles was the subject of a biographical sketch that appeared in the Sept. 21, 1960, issue of *Scope Weekly*. Given prominence in the article were her activities as founding president of the Pan American Medical Women's Alliance, former president of AMWA, and also her talents as rug-maker and stamp collector.

Dr. Frances L. Ilg, Director of the Gesell Institute of Child Development, was featured in an article in *Scope Weekly*, Feb. 24, 1960. Dr. Ilg, described as "clinician, researcher, author, and newspaper columnist," was associated with Dr. Gesell on the many books on the behavior of infants and children, and is coauthor of a recent book, "Child Behavior."

Dr. Olga Jonasson, winner of an AMWA Scholastic Honorable Mention Citation in 1958, has become the first woman surgical resident at the Research and Education Hospital of the University of Illinois. She received her appointment in July, 1960, after spending a year as research assistant in the Hospital's Department of Surgery.

In Iraq, an extensive government program of maternal and child care services, in which the United Nations Children's Fund is cooperating, is being headed by an American-

trained woman physician, DR. SALMA SHAIKH NURI. Dr. Nuri will be concerned with implementing the "bill of rights for children" recently proclaimed by the government of Premier Abdul Karim Kassim. The bill of rights guarantees health and educational services.

"Physical Examination of the Newborn," a medical film by DR. MARY D. OLNEY of the University of California, was shown to the clinical meeting of the AMA in Washington in November. The film was sponsored by Pfizer Laboratories.

DR. JEAN JONES PERDUE, the recently installed President of the Heart Association of Greater Miami, Florida, and the first woman to hold this position, stated that women will be the cause of decrease in major health problems because of their ability to educate the public and raise funds for research.

DR. RUTH PICK, Assistant Director of the Michael Reese Medical Center, Chicago, appeared in a photo on the front page of *Scope Weekly*, Aug. 10, with three students doing volunteer research work. Both students and physicians involved in the summer programs have echoed praise for the experience they received in this program.

DR. EDITH L. POTTER, on the staff of the University of Chicago Medical School, was one of the lecturers to appear before high school seniors who had indicated an interest in the study of medicine.

At the Conference on New Diuretics and Antihypertensive Agents held May 5-6 under the auspices of the New York Academy of Sciences, Section of Biological and Medical Sciences, DR. BARBARA RENNICK of Syracuse University spoke on "Animal Pharmacology of the Newer Diuretics—Benzothiadiazines, Spirolactones, Phthalimidine."

DR. GRACE M. ROTH, Consultant, Vascular Laboratory, Lovelace Clinic, Albuquerque, N. Mex., was a discussion leader of a fireside conference, "Role of Adrenals in Hypertension," at the American College of Chest Physicians' twenty-sixth annual meeting in Miami Beach, Fla., June 8-12.

The following women physicians recently received promotions (the first two listed) and appointments at Temple University Medical Center, Philadelphia: MARTHA E. SOUTHARD, Associate Professor of Radiology; MARY R. WESTER, Assistant Professor of Anesthesiology; HERTA MARIA SCHROM, Associate Professor of Pediatrics, and ROBERTA M. SHERWIN, Instructor in Internal Medicine.

DR. MILDRED LAW SNYDER of Middletown, Ohio, was honored last year by the Oxford, Ohio, Chamber of Commerce and the Oxford Press, and was presented with an inscribed silver tray. A local newspaper report noted, "It is believed that over 100 infants have been named 'Mildred' in her honor."

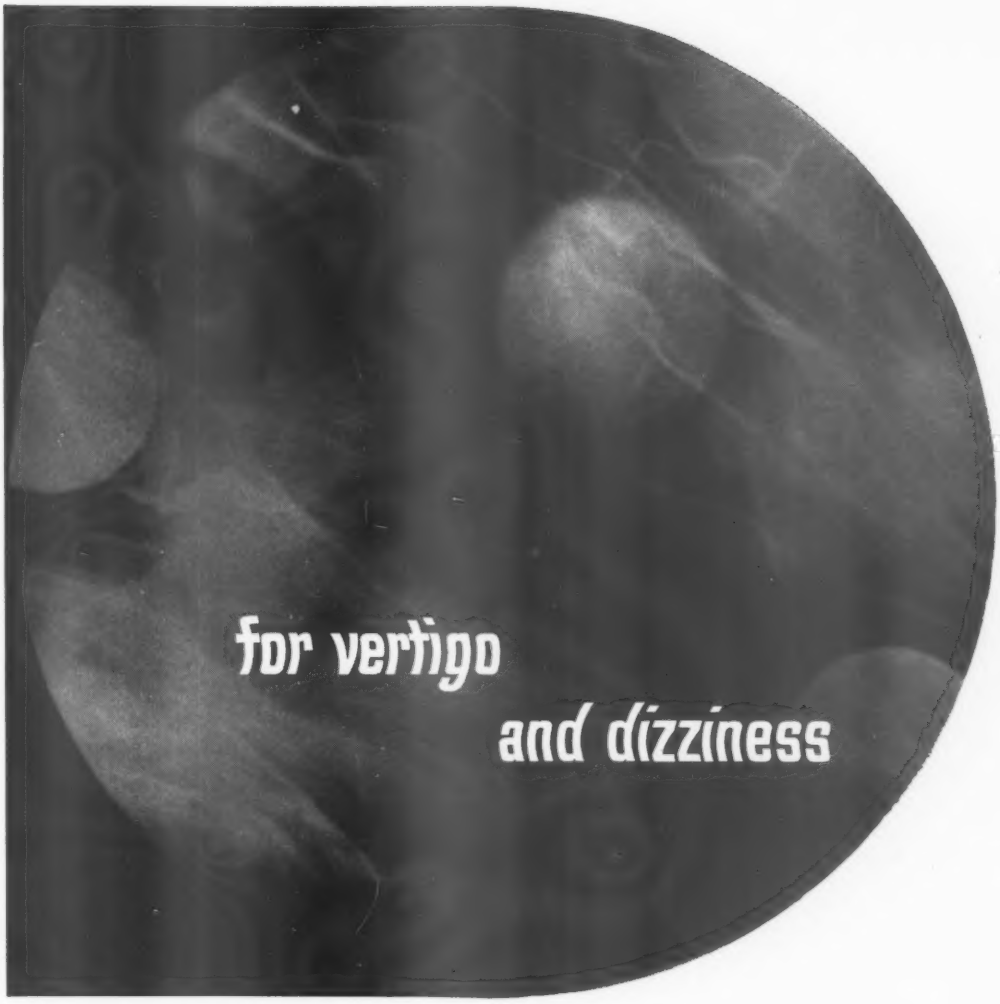
DR. PRISCILLA WHITE, Assistant Professor of Pediatrics at Tufts Medical School and member of the Joslin Clinic in Boston, gave the annual Banting Memorial Lecture at the twentieth annual meeting of the American Diabetes Association. Her subject was "Childhood Diabetes: Its Course and Influence upon the Second and Third Generations."

Branch News

A mock trial, "The Doctor Takes the Witness Stand," was held in October, 1960 by BRANCH TWO, CHICAGO. Local educators, dentists, and members of the Women's Bar Association participated in the program. Branch Two's November meeting featured a talk by Mr. John Ott on "Similar Growth Responses of Plants and Animals to Variations of Light Energy."

"Prevention and Control of Infections" was discussed by two physicians at the Branch meeting for January. Drs. Natalie Shuckmell and Mack Lepper were the speakers. In February members of the Branch will hear Drs. Pauline Cooke and Andree Zalis, presenting "Recent Advances in Electroencephalography."

Winning research papers entered by residents, interns, and senior medical students in a contest sponsored by the Branch will be featured on the April program. The 95th Anniversary of the Mary Thompson Hospital will be commemorated at the same meeting. Branch Two's formal program for the year will conclude with the annual meeting and installation of officers in May.



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dimenhydrinate with *d*-amphetamine sulfate

controls symptoms . . . improves mood

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Against the "Vaginitis Spectrum"

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A welcome clinical advance...
effective medication
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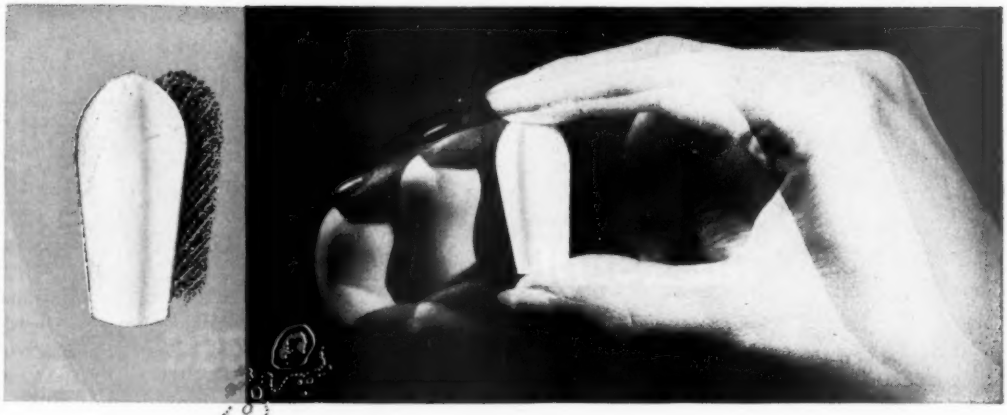

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COVERS CERVIX AND VAGINAL WALL—The pliant Milibis suppository disintegrates readily and molds itself to the cervix as well as the columns and rugae of the vaginal vault.

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with applicator.

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mother looks to you

Baby's first cereal can be his introduction to adult eating—an experience which can help set good eating habits for the rest of his life. Mother looks to you for help in making the right diet choices for her infant. Your advice is as important as it was when you prescribed his first formula.

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PABLUM brand cereals are formulated especially to fill the infant's needs for important minerals—especially iron—and for proteins, vitamins, carbohydrate, and calories. Available in five varieties—Rice, Mixed, Oatmeal, Barley, and High Protein—PABLUM cereals are highly useful in taste training.

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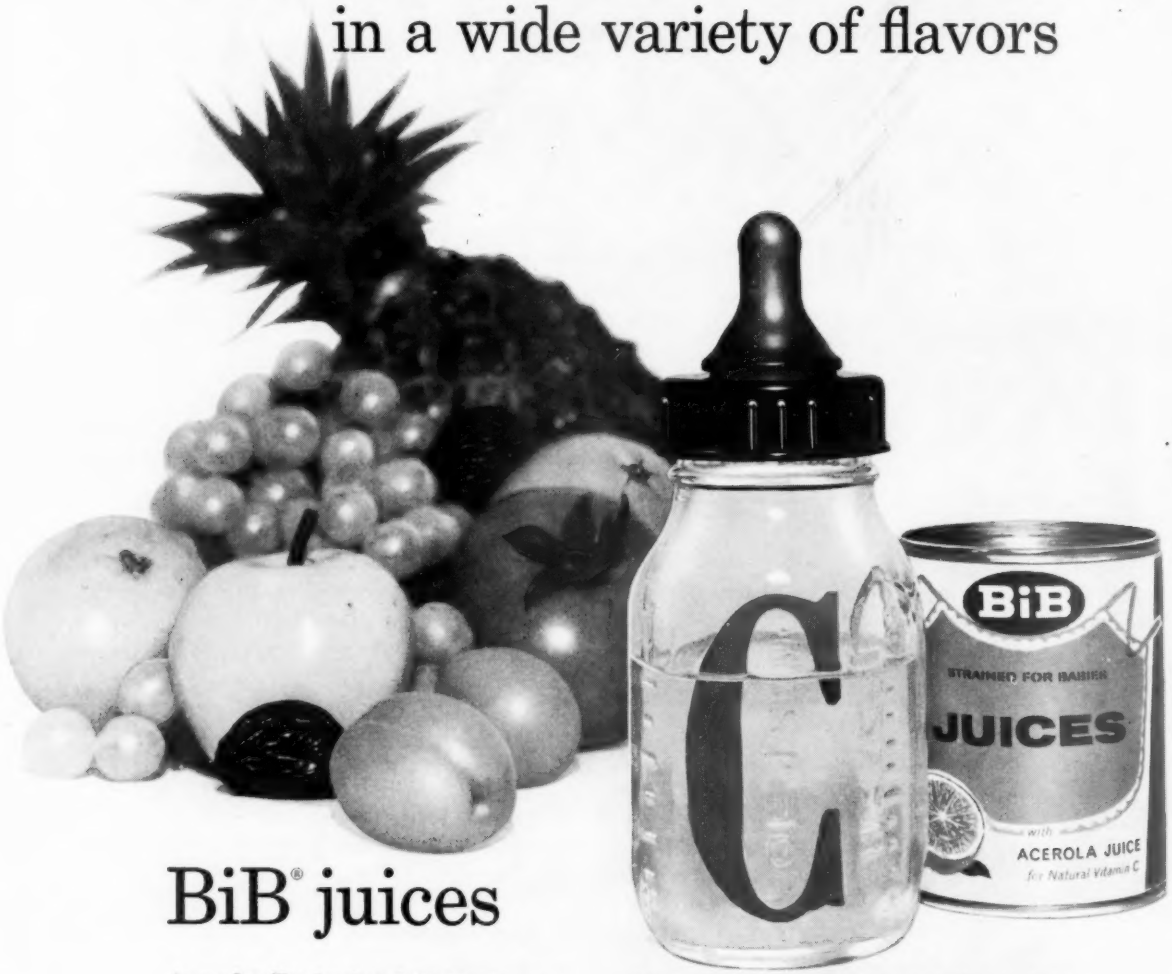

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Hypoallergenicity and improved tolerance are achieved through special processing which reduces the seed protein and peel oil content to negligible quantities. In a clinical study with Acerola, "No reactions occurred from ingestion or from skin and intradermal tests with Acerola juice."[2]

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BiB juices permit early introduction of a wide variety of flavors—valuable in taste-training the infant. Special process assures free flow through bottle nipple; ideal for spoon or cup feeding, too. BiB juices require no reconstitution, no heating, no defrosting. All mother does is open the can of BiB juice and it's ready for feeding.

References: (1) Asenjo, C. F., and Freire de Guzman, A. R.: Science *103*:219 (Feb. 22) 1946. (2) Clein, N. W.: J. Pediat. *48*:140-145 (Feb.) 1956.

335R60

Mead Johnson
Symbol of service in medicine

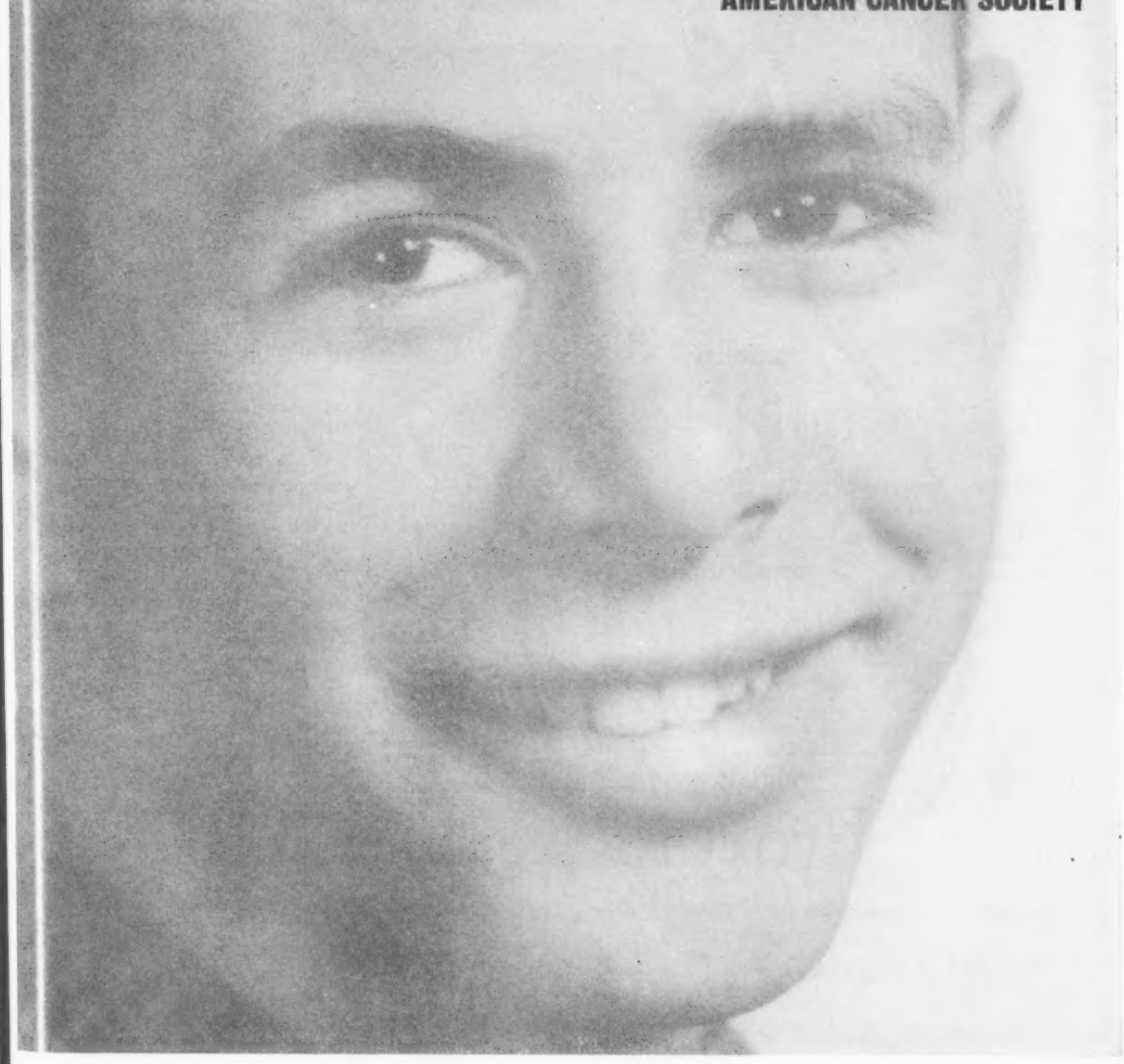
MORE THAN A MILLION AMERICAN SCHOOL CHILDREN ARE DOOMED TO EVENTUAL DEATH FROM LUNG CANCER IF PRESENT TRENDS CONTINUE. The American Public Health Association made this prediction last Fall and called upon "health authorities to undertake a broad educational effort, especially among young people, to prevent cigarette smoking."

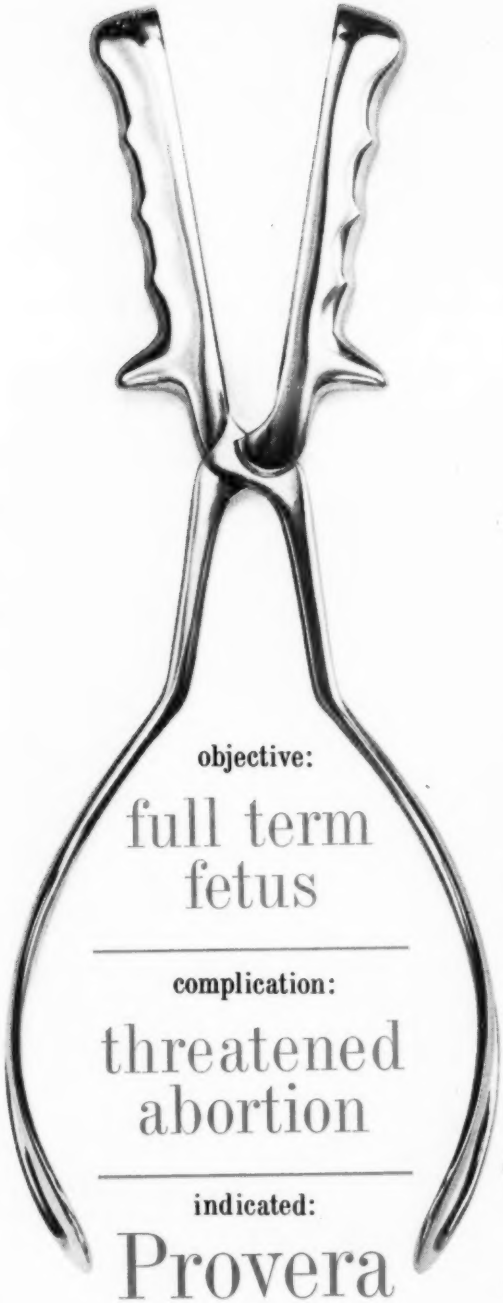
How is this to be done, doctor? As a partial answer, the American Cancer Society has produced a filmstrip, TO SMOKE OR NOT TO SMOKE, based on a recently completed study of thousands of high school students. Intended for presentation in high school classrooms, this filmstrip is available from the Society's 60 Divisions throughout the country.

But the effectiveness of this educational tool will depend on the support of the entire community—teachers, parents and, most of all, physicians. Many physicians are already lending their support by participating in the presentation of the filmstrip.

This is another example of how the medical profession and the American Cancer Society can cooperate in essential public education in the fight against cancer.

AMERICAN CANCER SOCIETY





objective:

full term fetus

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Depo-Provera**

Sterile micronized medroxyprogesterone acetate (17-alpha-hydroxy-6-alpha-methyl-progesterone acetate). 50 mg. per cc. in 1 cc. and 5 cc. size vials.

For premenstrual tension Provera plus diuretic plus tranquilizer adds up to logical therapy. Each Cytran** tablet contains 2.5 mg. Provera, 3.5 mg. Cardrase* (ethoxzolamide), and 300 mg. Levanil* (ectylurea).

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prevention of "next-morning sickness" with a single bedtime dose

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a record of effectiveness, excellent toleration, and economy

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INDICATIONS: Valuable in the symptomatic relief of nausea and vomiting of pregnancy. Also indicated for motion sickness, radiation sickness, vertigo associated with Ménière's syndrome, labyrinthitis, fenestration procedures, vestibular dysfunction, and dizziness associated with cerebral arteriosclerosis.

ADMINISTRATION AND DOSAGE: For control of nausea and vomiting of pregnancy, a single dose of 25 to 50 mg. at bedtime is usually effective. For dosage schedules in other indications, see package insert.

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Time present and time past
Are both perhaps present in time future.
—*T. S. Eliot*

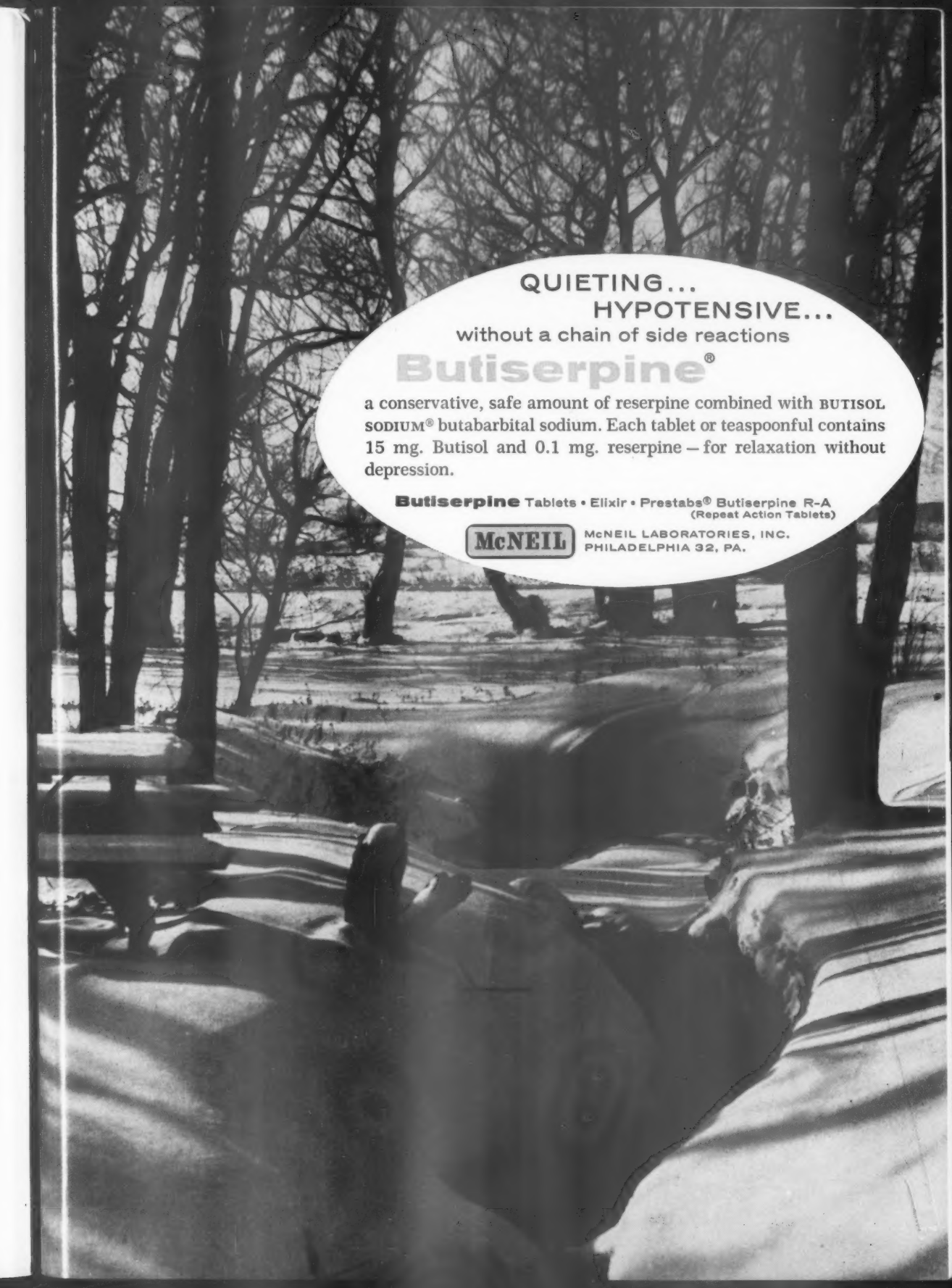
The American Medical Women's Association takes great pleasure in extending congratulations to its member,

Dr. Janet Grame Travell,

on her recent appointment as personal physician to the President of the United States, John F. Kennedy.

"The choice of Dr. Travell as White House physician is another proof of the growing appreciation, in this country, of the role of women in medicine. This should give to other young women who are considering a medical career added strength in their resolve to enter this profession."

—Claire F. Ryder, President
AMWA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A slight upward adjustment of Orinase dosage is often the only step needed to establish or regain optimum control of diabetes. The increase serves to make available the amount of Orinase-released native insulin *required* by the patient. The change may be made freely, to 3 grams or more a day, because Orinase has virtually no "ceiling" imposed on dosage by toxicity or untoward effects.

To maintain smooth control, to avoid needless "secondary failures," give sufficient Orinase to meet the varying needs of different patients or the varying needs of an individual patient.

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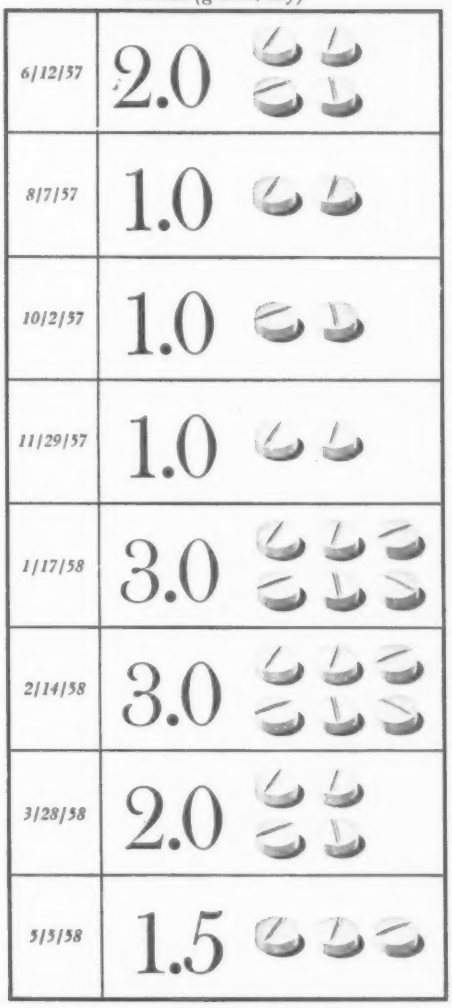

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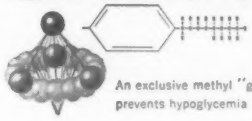

An exclusive methyl "governor" prevents hypoglycemia

American Medical Women's Association, Inc.

BRANCH OFFICERS, 1960-1961

(Continued from Page 32)

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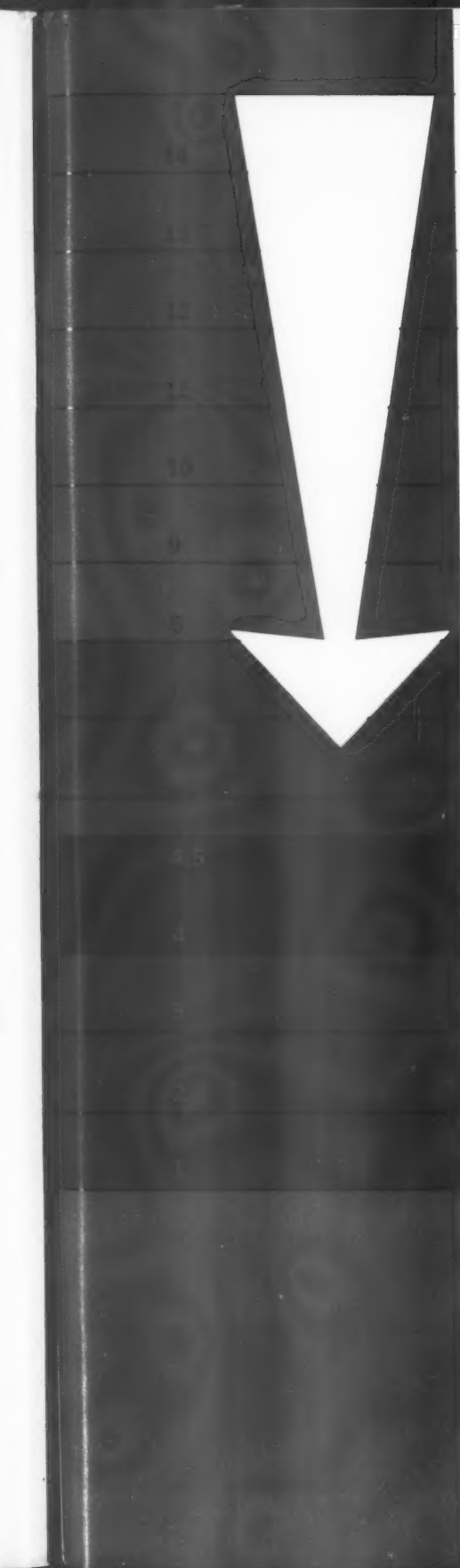

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INDEX TO ADVERTISERS

Abbott Laboratories 19-20
Ayerst Laboratories 31
Eaton Laboratories ..... 11, 25, 80, Inside Back Cover
The Fesler Company, Inc. 29
Lederle Laboratories 15, 28
Eli Lilly & Company 36
McNeil Laboratories, Inc. 8, 79
The S. E. Massengill Company 84-85
Mead Johnson ..... 9, 73, 74, Back Cover
Merck Sharp & Dohme 83
Ortho Laboratories 6
Parke, Davis & Company 17
Pfizer Laboratories 77
Riker Laboratories ..... Inside Front Cover, 10, 88
Roche Laboratories 4, 34-35
J. B. Roerig & Company 22-23
G. D. Searle & Company 3, 71
Smith, Kline & French 21
Tassette, Inc. 33
Upjohn Company 26-27, 76, 81
Whittaker Laboratories, Inc. 86
Winthrop Laboratories 12-13, 72

INDEX TO PRODUCTS ADVERTISED

ANALGESICS
Darvon *(Lilly)* 36
Trancoprin *(Winthrop)* 12-13
Tylenol *(McNeil)* 8

ANTACIDS
Titralac *(Riker)* 88

ANOREXIGENIC AGENTS
Didrex *(Upjohn)* 81
Metrecal *(Mead Johnson)* 9

ANTIBACTERIAL AGENTS
Furacin Cream *(Eaton)* 80
Furadantin *(Eaton)* ... Inside Back Cover

ANTIBIOTICS
Declomycin *(Lederle)* 15
Maxipen *(Roerig)* 22-23
TAO *(Roerig)* 22-23

ANTIEMETICS
Bonine *(Pfizer)* 77
Dramamine *(Searle)* 71
Tigan *(Roche)* 34-35

ANTIHYPERTENSIVE AGENTS
Butiserpine *(McNeil)* 79

ANTIPYRETIC AGENTS
Tylenol *(McNeil)* 8

ANTITUSSIVE AGENTS
ULO Syrup *(Riker)* .. Inside Front Cover

BABY FOODS
Bib Juices *(Mead Johnson)* 74
Pablum *(Mead Johnson)* 73

CONTRACEPTIVES
Cooper Creme*(Whittaker)* 86
Delfen *(Ortho)* 6
Preceptin *(Ortho)* 6

DIETARY SUPPLEMENTS
Vi-Daylin *(Abbott)* 19-20
Viterra *(Roerig)* 23

DIURETICS
Cyclex *(Merck Sharp & Dohme)* 83

HEMATINICS
Ferro-Sequels *(Lederle)* 28

HORMONES
Cytran *(Upjohn)* 26-27
Norlutin *(Parke, Davis)* 17
Orinase *(Upjohn)* 81
Premarin *(Ayerst)* 31
Provera *(Upjohn)* 76
Vallestril *(Searle)* 3

MENSTRUAL AIDS
Tassette *(Tassette)* 33

MYOVASCULAR RELAXANTS
Vasodilan *(Mead Johnson)* ... Back Cover

STOOL SOFTENERS
Ferro-Sequels *(Lederle)* 28

TRANQUILIZERS
Butiserpine *(McNeil)* 79
Deaner-100 *(Riker)* 10
Stelazine *(Smith, Kline & French)* 21
Trancoprin *(Winthrop)* 12-13

URETHRAL SUPPOSITORIES
Furacin Inserts *(Eaton)* 11
Furestrol Suppositories *(Eaton)* 11

VAGINAL THERAPEUTICS
Massengill Powder *(Massengill)* 84-85
Milibis *(Winthrop)* 72
Trib *(Roche)* 4
Triburon*(Roche)* 4
Trichotine *(Fesler)* 29
Tricofuron *(Eaton)* 25

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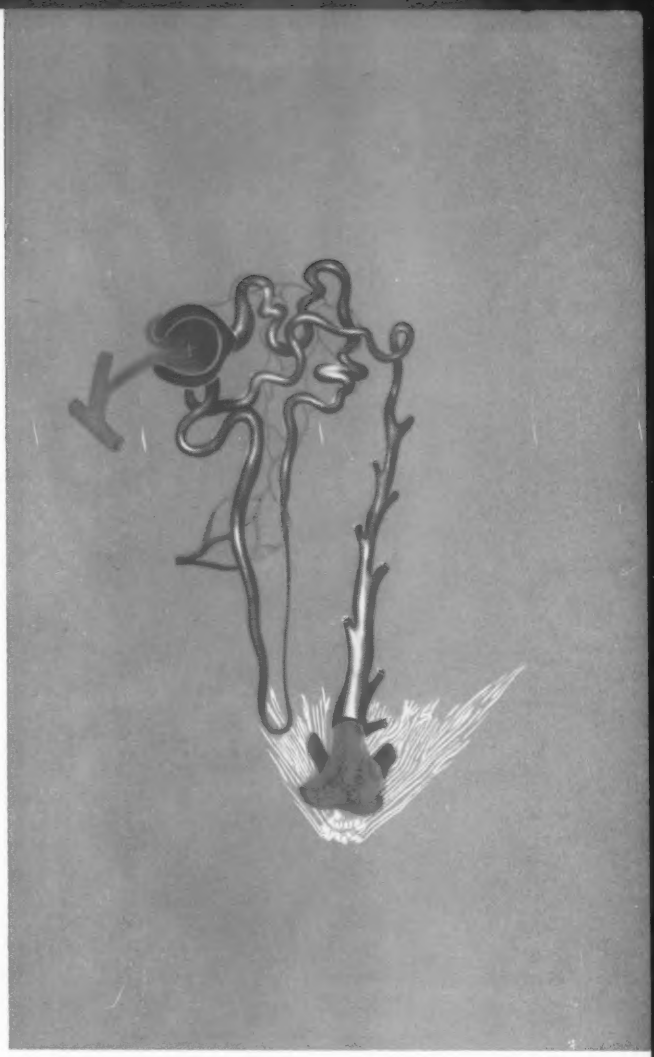

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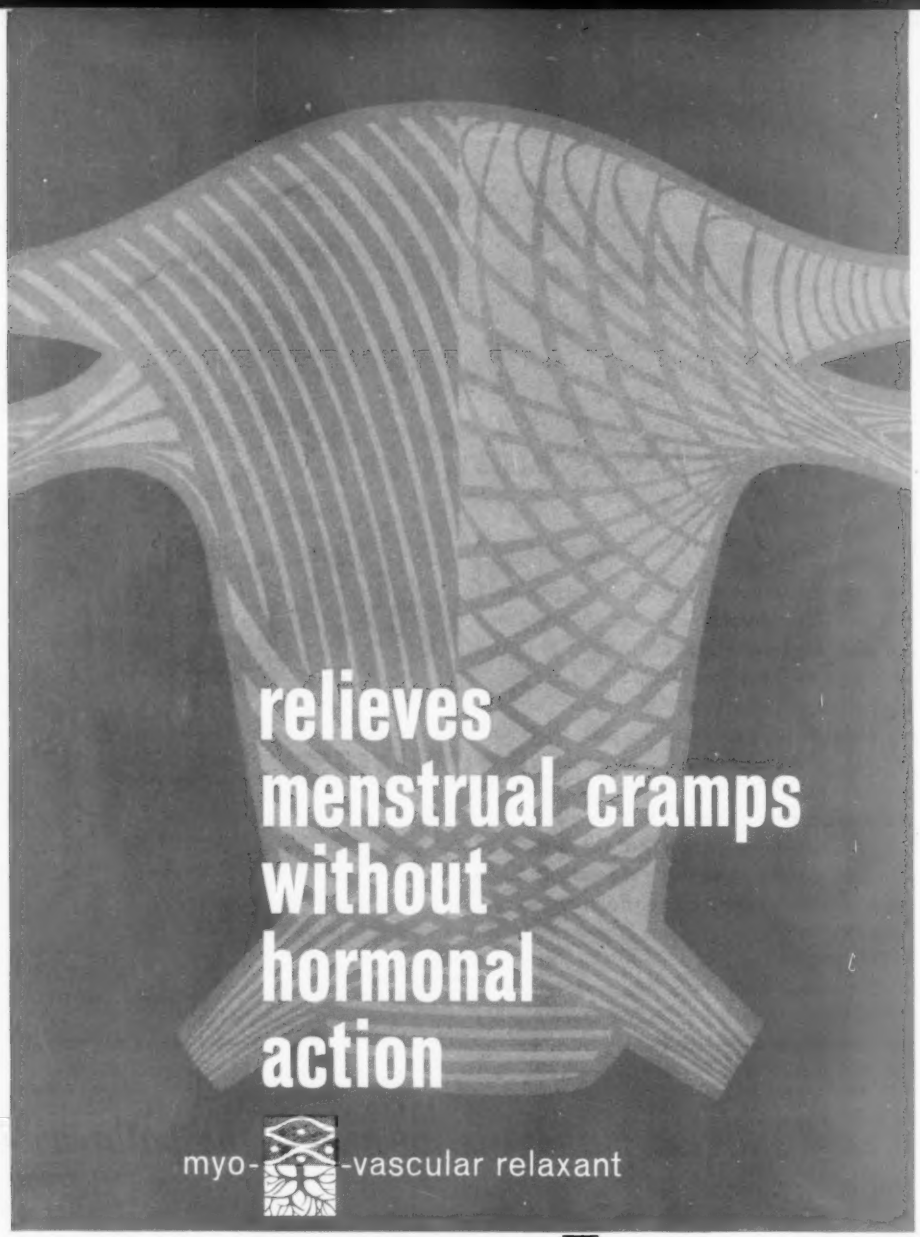

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